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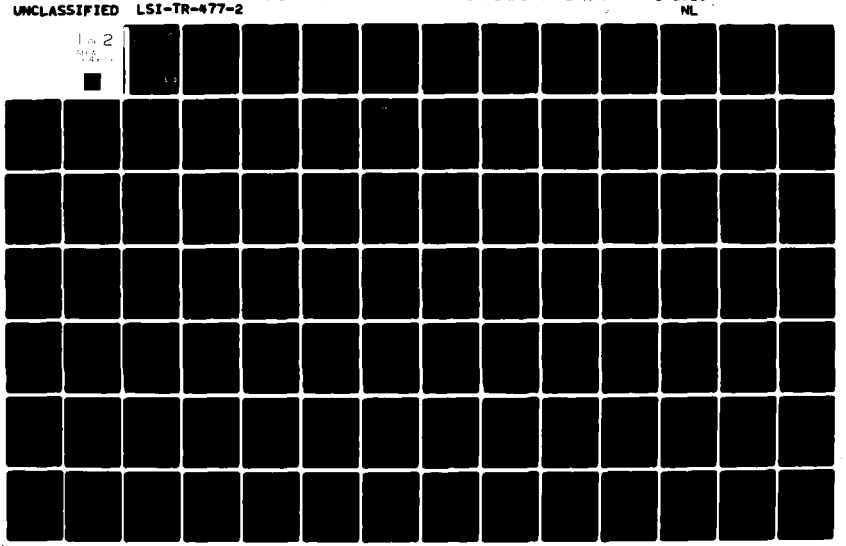

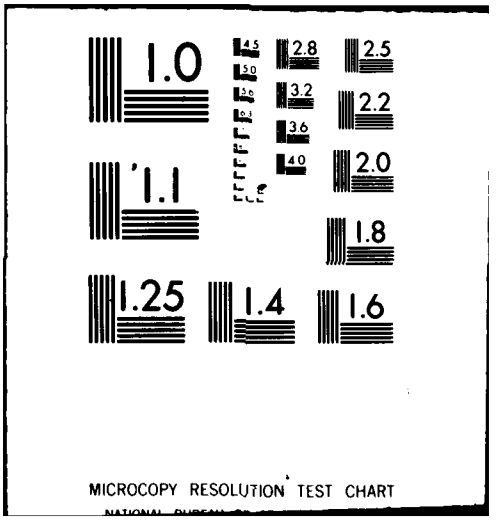
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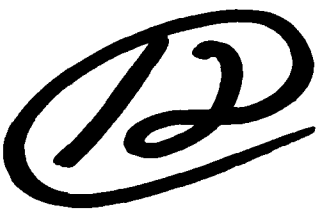

LSI TR-477-2

MAMMALIAN TOXICOLOGY TESTING: PROBLEM DEFINITION STUDY

COMPARATIVE ANALYSIS REPORT (U)

by
R. A. Wynveen, R. H. Reuter,
and R. J. Davenport

March, 1981

Supported by
U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701

Contract DAMD17-81-C-1013

Life Systems, Inc.
Cleveland, OH 44122

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

Global Army mammalian toxicology testing requirements were defined, and to some extent those that would be the responsibility of the U.S. Army Medical Research and Development Command (USAMRDC) were identified. Since no quantitative or qualitative description of the Army's toxicology capability exists, the unmet requirements could not be precisely defined. Approaches for meeting a portion of the USAMRDC's unmet requirements were compared and particular emphasis was placed on production testing for mammalian toxicology studies.

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Evaluation Criteria, Immediate Toxicology Requirements, Toxicology Testing Regulations Impact, Sources for Toxicology Testing, Locations for Army Toxicology

20. Continued-

The cost to fulfill unmet requirements will approach $30 million per year for the global Army, and if it is assumed that 30 to 60% of the requirements are the responsibility of the medical organizations, their annual budgets would need to be increased by $10 to $20 million. Funding should not be diverted from other MRDC priority programs. Additional capability and capacity for toxicology testing should be added only after balancing and specifying requirements, resolving responsibilities and obtaining budgetary commitments.

Reports for the subject contract include three major final reports and twelve supporting documents. Specific conclusions and recommendations concerning facilities, priorities, and planning are provided. The methodology developed to evaluate the Army's toxicology requirements should also be useful as a model for additional recommended studies.

EXECUTIVE SUMMARY

The purpose of the Comparative Analysis portion of the Problem Definition Study was to assist the Army in identifying a portion of its global toxicology requirements and to provide information which will help in a comparison of the alternative options for meeting U.S. Army Medical Research and Development Command's unmet portion of those requirements.

The Army's Toxicological Requirements

Complexity of the Problem

The Army's toxicological requirements are considerably more complex than those confronting even the largest industrial corporations, for two major reasons:

- The Army is an integrated conglomerate of many businesses and is engaged in at least ten major industries
- The Army is not only a materiel developer but is also the distributor, maintainer, user and disposer of the materiel it develops

When viewed in light of the size of the Army's operations ($40 billion annually), the task of identifying, categorizing, quantifying and planning to resolve its toxicological requirements is somewhat staggering to contemplate. Yet contemplate it we must, and this Problem Definition Study was an important step in this process. The numbers of requirements are large; they are mostly unaddressed and are quite diverse. The responsibility for control is divided among several organizations and the information that needs to be reviewed to identify requirements is reported in many documents with different reporting periods.

Meeting toxicological requirements is a unique, lengthy and costly process. To carry out, for example, the compliance protocol for a single chemical requires three to five years and $3 to 5 million, and even after all that, the regulatory interpretation and acceptance of the data are outside the Army's control (There are no shortcuts.) Testing time cannot be reduced by adding more money or people, and cost is a direct result of complying with prescribed protocols. And finally, toxicology cannot solve a crisis that has already happened. It can only clarify the extent of the crisis and provide information which may preclude a future one. These unique aspects of meeting toxicological requirements can be frustrating and must be taken into account by those who will be deeply involved.

The Army's requirements are the sum of requirements arising from several sources such as regulatory (laws and executive orders); nonregulatory (soldier performance, disability compensation, litigation, etc.); the need for data for permits and licenses, drug and vaccine development, Army production plants, field training and combat; and the need to develop testing methodology for Army-unique materiel and environments. At least 15 major public laws, for example, relate to toxicology and impact on the Army in areas such as air, water and land pollution; toxic substances; occupational safety and health; transportation of hazardous materials; and radioactive materials. These laws affect the entire life cycle of Army materiel including Research, Development,

Test & Engineering manufacturing, transportation, inventory, training, combat and demilitarization. Many of the Army's unmet requirements arise out of recent changes in toxicology laws and out of increasing awareness of the toxicological hazards of chemicals and their applications.

Levels of Toxicological Capability

There is a wide range of toxicological capability levels from production type testing using standard protocols to full-service capability. The latter concept embraces all the levels and all the scientific disciplines within the scope of toxicology such as behavioral, metabolism, pharmacokinetics, pharmacodynamics, oncogenic, respiratory physiology, reproduction, teratology, neurotoxicology. The Army needs full-service capability because, in part, of the many Army-unique requirements, but also because more than testing must be done to determine what to control, to optimize the amount of testing, prioritize requirements, validate results, implement necessary controls and perform necessary follow up. The term "full-service" capability includes--in addition to all the toxicological disciplines--a wide variety of pre-testing, parallel-with testing, and after-testing activities. More than 30 such activities are identified in Appendix 4 of the report.

Although some of the Army's toxicological requirements are already being met (such as drug and vaccine development, offensive chemical warfare agents, defensive biological warfare agents, nuclear warfare, etc.), most remain undone:

- Developing a process for identifying unmet toxicological requirements
- Quantifying the capability and capacity of existing U.S. Medical Research and Development Command toxicological facilities
- Determining who is responsible for meeting which requirements, and obtaining funding commitments to pay for them
- Identifying non-Army capabilities which should provide support or services and negotiating the terms of such relationships
- Developing a master plan which takes all the key issues into account, prioritizes implementation actions and assures that necessary funding will be available

Additional significant recommendations are also contained in the report.

Methodologies for Identifying Unmet Requirements

The Study Team simultaneously pursued different sources of information for identifying Army toxicological requirements. They reviewed the Department of the Army's overall budget, procurements budget and Research, Development, Test and Engineering budget for several years; the Catalog of Approved Requirements Documents; documents involving U.S. Army Medical Research & Development Command efforts (including 14988 Forms); The Army Weapons System Booklet; the description of the Army's Research, Development, Test & Engineering Weaponry; toxicology being done by U.S. Medical Bioengineering Research & Development Laboratory

(via 1498's), Chemical Systems Laboratory and Army Environmental Hygiene Agency; and a large number of additional pertinent documents and reports.

The Team developed a three-dimensional method for viewing the Army's toxicological requirements which takes into account the materiel requirements itself, changes in requirements over the materiel's life cycle and the specific toxicology service requirements involved (of which only part is associated with testing). Use of this approach helps to systematize the task of identifying requirements and to assure that major requirements are not inadvertently overlooked.

Within this context, the Team then identified 13 different approaches to defining toxicological requirements. Each approach will identify some requirements and miss others. Each also has a different cost, both in time and in money. Six of these methods were judged by the Team to be key approaches which should be used in any analysis of Army toxicological requirements. Their principal characteristics are summarized as follows:

Approach	What It Will Identify	What It Will Miss	Price	
			Cost	Time
Top Down	RDT&E and Procurement	Inventory, existing plants	Med	Long
Talking to DARCOM PM's	50 Major Programs	Many minor Programs; Uses	Low	Med
Legalistic	Regulator	Nonregulator; What's in Lab.	Med	Med
Manufacturing Process Review	Starting, Intermediate, final & byprods.	Applications; Uses	Med	Med
Questionnaires	Known & Some Unknown	Hard to Find	Low	Med
Life Cycle Network	New Materiel	Inventory	Med	Long

The report describes each of the 13 methods in detail and under what circumstances each should be used.

Quantification of Requirements

To develop a first approximation of the Army's toxicology requirements, the Study Team performed a detailed review of the Army's chemicals, weapons and manufacturing plants. Almost 1,700 chemicals were estimated to be in the Research, Development, Test & Engineering cycle, 200 weapons were found to potentially represent toxic hazards and more than 20 plants have probable testing requirements. Applying the cost estimates developed by the Team, and including before-testing, parallel-with testing and after-testing toxicology tasks as well as the testing itself, annual costs of about $40 million were

calculated. This is believed to represent about 50 percent of the Army's total requirements which are estimated, therefore, to be about $80 million per year. Estimating unmet requirements at 60 percent of this total, and testing as 60 percent of the unmet requirements, then total unmet testing requirements are about $30 million annually. Deleting chemical agents and drugs and vaccines from this leaves a total of about $28 million.

The Army's toxicology requirements can be expected to continue indefinitely. There is a significant backlog of requirements to be met. But even after the "bow wave" of requirements is handled, the Army faces needed requirements associated with the life cycle of materiel: its development, manufacturing, transportation, storage, training, use and disposal.

Comparative Analysis of Alternative Approaches

There are many existing sources of toxicology testing, not all of which, however, are suited to the Army's needs. Those which potentially have value to the Army are identified in the report.

Four basic approaches (plus combinations of the four) were investigated by the Study Team:

- GOGO (Government-Owned, Government-Operated)
- GOCO (Government-Owned, Contractor-Operated)
- COGO (Contractor-Owned, Government-Operated)
- COCO (Contractor-Owned, Contractor-Operated)

There are also a number of variations of these basic types. Between GOGO and GCCO, for example, there are actually five additional possibilities:

Operator			
Business	Technical		Business and
Only	Prof. Only	Tech.Only	Technical
--	--	--	Government
Government	Government	Contractor	--
Government	Contractor	Contractor	--
Contractor	Government	Government	--
Contractor	Government	Contractor	--
Contractor	Contractor	Government	--
--	--	--	Contractor

This demonstrates that the control of a GOCO can be at whatever level U.S. Army Medical Research and Development Command desires to best meet its end product, cost and schedule goals.

Several major criteria were identified for comparing alternatives:

- Capability for handling Army-unique requirements
- Acceptability of results

- Minimal government personnel required
- Flexibility to change volume
- Effect on Army's smart buyer ability and organizational memory
- Protecting confidentiality of results
- Speed of response to new requirements

A number of minor criteria were also developed such as the ability to monitor Quality Assurance and the time required to implement the selected approach needed.

A cost analysis revealed that GOGO's and GOCO's will cost about 20 percent less than COCO's because of overhead, G&A and fee factors. The cost analyses were based, in part, on detailed cost information developed for four general toxicology tests by the Study Team (see Appendix 11).

Using the above criteria and cost estimates, a qualitative assessment was made of the four basic approaches. Over the short term, e.g., 5 years, COCO's are best, then COGO, GOCO and GCGO. In the long run, e.g., 10 years or more, however, the GOGO approach is best, then GOCO, COGO and COCO. The poor long-term ranking of COCO's is because of their failure to provide smart buyer and memory capability to the Army. The analysis also showed that a single performance mechanism cannot handle the Army's requirements. A combination of in-house and external sources will be required.

Other Studies

A nmber of special projects were undertaken by the Study Team and are described in the report. Among them were:

- The approvals needed to initiate construction
- Load-leveling techniques
- Handling peak demands for certain key personnel (such as veterinary pathologists)
- Testing that could be started immediately (through COCO's)
- The time needed (4 to 7½ years) to get ready for testing if renovation or new construction is needed
- That a remote site for hazardous testing is attractive in concept but is not cost effective and would be difficult to staff
- The effect of maintenance costs (very minor) on selection of testing options
- The pros and cons of doing toxicological testing for other DOD agencies

Other Conclusions

In addition to those itemized in this Executive Summary, the Study Team reached a number of additional conclusions and made certain additional recommendations:

- A decision is needed to implement a program to meet U.S. Army Medical Research and Development Command responsibilities for is unmet toxicology requirements. The first step in such a program is to develop a comprehensive plan.
- A decision is also needed as to whether U.S. Army Medical Research and Development Command is the logical focal point for the Army's non-medical toxicology testing.
- Do not proceed with building a toxicology testing facility until after other decisions made.
- There are several ways in which responsibility for toxicology can be assigned--to the equipment developer (e.g., DARCOM), to the test and evaluation organizations or to the Army Medical Department (AMEDD).
- A single lab such as U.S. Medical Bioengineering Research & Development Laboratory cannot effectively handle all the Army's toxicology needs.
- No capabilities for the Army's unique inhalation requirements exist. Such a facility should be developed as an Army capability. It should be designed to do more than just toxicology testing.
- A number of questions remain to be answered before decision can be made as to what kind of organization (GOGO, GOCO, etc.) the inhalation facility should be.

FOREWORD

A Mammalian Toxicology Testing Problem Definition Study was conducted for the U.S. Army Medical Research and Development Command, Ft. Detrick, Frederick, MD, under Contract DAMD17-81-C-1013. The Study's Principal Investigator was Dr. R. A. Wynveen. COL Alfred M. Allen, Toxicology Project Officer, Letterman Army Institute of Research, was the Contracting Officer's Technical Representative. Mr. Michael F. Travis was the Contracting Officer's Representative. Ms. Jean Smith was the Contracting Officer.

Results of this study were published in three Final reports. Reports for this Contract, DAMD17-81-C-1013, consist of three major final reports and twelve supporting documents. The contract title, MAMMALIAN TOXICOLOGY TESTING: PROBLEM DEFINITION STUDY, is the main title for all the reports. Individual reports are subtitled and referenced with Life Systems, Inc. report numbers as detailed below. Please note that the Life Systems report numbers in text references are shortened. In the Defense Technical Information Center (DTIC) data base the reports are identified by the complete report numbers (i.e., LSI-TR-477-XXX) and complete numbers must be used for retrieval.

Report Subtitle	Life Systems, Inc. Report Number
Final Reports--	
Part 1. Comparative Analysis Report	LSI-TR-477-2
Part 2. Facility Installation Report	LSI-TR-477-3
Part 3. Impact of Future Changes Report	LSI-TR-477-4
Supporting Documents--	
Technology Changes Impact on Testing Requirements	LSI-TR-477-14
Quality Assurance Plan	LSI-TR-477-17A
Capability Modules	LSI-TR-477-19B
Technical Plan	LSI-TR-477-20A
Equipment Plan	LSI-TR-477-21A
Personnel Plan	LSI-TR-477-23A
Inhalation Chambers and Supporting Equipment Survey	LSI-TR-477-26A
Equipment List for Modules	LSI-TR-477-28B
AMTR Protocol/Pricing Report	LSI-TR-477-29A
Global Army Toxicology Requirements	LSI-TR-477-31A
Comparison Toxicology Test Costs	LSI-TR-477-36A
Annual Testing Capacity	LSI-TR-477-38A

This is the Comparative Analysis Report.

This contract supported technical efforts by Life Systems' personnel, various supporting organizations and consultants.

Support Life Systems' personnel included Mr. Richard Alban, Dr. Ron Davenport, Dr. Jack Glennon, Ms. Darlene Jones, Mr. Ron Kohler, Dr. Joel Lantz, Mr. Earl Linaburg, Ms. Pat Marcinko, Mr. Jim McFarland, Ms. Cynthia Patrick, Dr. Roy Reuter, Ms. Dorothy Ruschak, Mr. Greg Schiefer, and Dr. Rick Wynveen.

The participating supporting organizations included: ICAIR Systems, Inc. and Theodore Jonas/Associates LTD.

Participating consultants were Dr. Robert Drew, Dr. Wendell Kilgore, Dr. Keith Killam and Dr. Robert Tardiff.

Citations of organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

TABLE OF CONTENTS

continued-

Table of Contents - continued

continued-

Table of Contents - continued

LIST OF FIGURES

LIST OF TABLES

INTRODUCTION

Life Systems, Inc. (LSI), its Subcontractors and Consultants, completed a program entitled "Mammalian Toxicology Testing: Problem Definition Study" (Study). The program was divided into four major efforts:

1. A definition of the global Army's mammalian toxicology requirements.

2. A comparative analysis of approaches for meeting a portion of the unmet requirements that would be the responsibility of the U.S. Army Medical Research and Development Command USA (USAMRDC).

3. Preparation of plans for a model toxicology facility to implement a portion of the USAMRDC's unmet requirements.

4. A determination of the impact of changes in toxicology regulations and technology over the next ten years on the Army's toxicology requirements.

This document summarizes that portion of the Study associated with identifying the global Army's need for toxicology and a comparative analysis of options for meeting the USAMRDC's unmet portion of these requirements. Efforts three and four above are discussed elsewhere (Life Systems, Inc. 1981a[1], Life Systems, Inc. 1981b, respectively). The material contained in these reports will not be duplicated in the current report.

Study Objectives

The objectives of the Study were:

1. To assist the Army in identifying mammalian toxicology requirements and, if possible, establish a methodology that could continue to be used after the Study.

2. To assist the Army in identifying advantages and disadvantages of various options for carrying out mammalian toxicology, with particular emphasis on production testing.

3. To assist the Army in projecting the impact on Army requirements and planning of changes in toxicology related regulations and technology.

4. To assist the Army in determining the resources needed to add extra toxicology capability and capacity to that already available through USAMRDC.

5. To quantify the relative cost of various performance options.

The program was done extramurally because the USAMRDC staff was busy on other priority efforts.

(1) References are cited at the end of the report.

Definitions and Acronyms

Appendix 1 contains the definition of terms and acronyms used in this report or during the program.

Assumptions

Many of the assumptions used are cited at the beginning of each section. The remaining assumptions are generally contained in supporting documentation that has become part of the Study's data base.

Background

The initial thrust of the Study focused on the Army's needs for routine, production toxicology testing. During the early part of the program, however, the definition of toxicology testing was expanded to include applied mammalian toxicology research. The difference is discussed below.

Prior to the Study an effort was completed that evaluated the USAMRDC's toxicology requirements. It reflected a growing toxicology testing need. It further identified a major increase in the demand by others for a limited, albeit growing, toxicology testing capability. Following this Study, an evaluation was made concerning the Study's conclusions. One of these was that a new capability should be added for carrying out toxicology testing at an USAMRDC controlled facility (e.g., the Letterman Army Institute of Research (LAIR)) and operated by a contractor.

A team of USAMRDC personnel evaluated the conclusions of a report entitled "Report of Mammalian Toxicology Testing Requirements and Concepts for Solution" by R. H. Reuter dated 1979, USAMBRDL, and visited various national toxicology laboratories and laboratories owned by the Government and operated by contractors. This survey demonstrated that:

1. The requirements included in the initial Study did not encompass the global Army's.

2. The LAIR represented only one of several possible locations for any additional toxicology testing facility.

3. Although many government agencies are utilizing the Government-Owned, Contractor-Operated (GOCO) route for overcoming personnel ceilings, a direct comparison between alternatives is needed to select between alternatives.

For these and other reasons the current Study was initiated to be completed within three months. Subsequently, additional effort was added which extended the duration.

Why Mammalian Toxicology Needed?

There are many reasons why the Army has toxicology requirements. Besides complying or demonstrating conformance to laws and regulations, other reasons include generating data to obtain permits and licenses, obtaining approval to manufacture or continue to manufacture Army chemicals, as part of carrying out

effective drug and vaccine development processes, to develop testing methodologies for Army-unique environments and materiel and to establish standards and criteria for occupational health in Army laboratories, in Army production plants, in field training and for combat. Still other toxicology research or testing must be done because they are part of good business practices or for ethical and moral reasons.

Regulatory Requirements. The public laws and executive orders that require toxicology testing and affect a toxicology research/testing facility's design and operation are extensive. Appendix 2 contains a summary of the 15 major public laws relating to toxicology, references to two executive orders relating to toxicology requirements and a 1979 status of the foreign toxic substances laws the Army encounters. These laws and executive orders affect the Army's activities associated with hazardous and toxic substances: Insecticide, fungicide and rodenticide development and manufacture; munitions manufacture; food, drug and cosmetic development, occupational safety and hazard avoidance; etc.

Figure 1 illustrates the impact legislation has on the Army's materiel during the entire life cycle from the research, development, test and engineering (RDT&E) phase into manufacturing, transportion, inventory, training, and combat and finally during demilitarization.

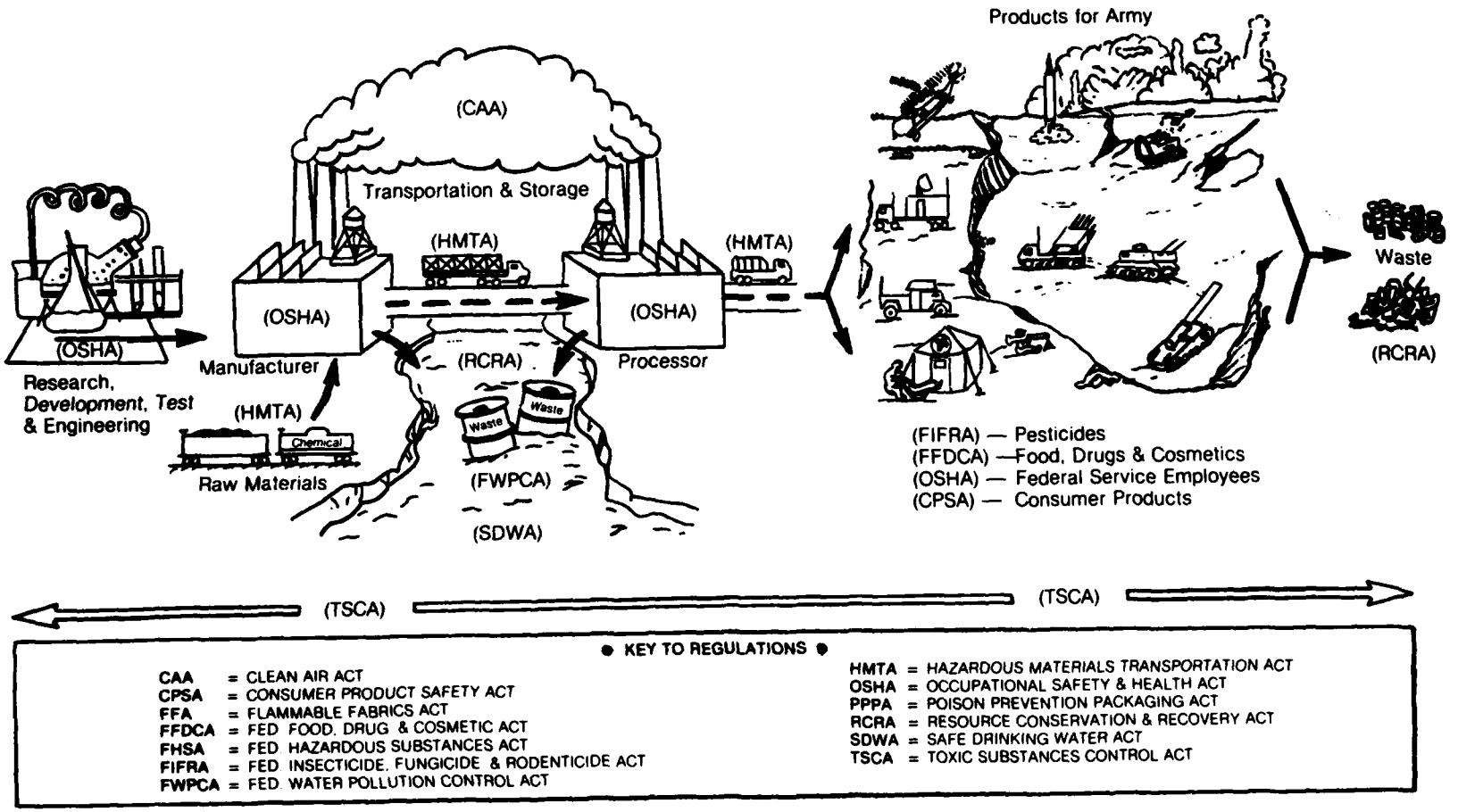
The effects of just one section (8(e)) of the Toxic Substance Control Act (TSCA) can have a very large impact on the Army's toxicology requirements. Various internal considerations and reporting requirements will result from:

Process Modifications (preceeded by reviews and evaluations)
Process Withdrawal (preceeded by reviews and evaluations)
Reformulations (in cases of mixtures -- relates to identification of causative agent(s))
Product Modifications (preceeded by reviews and evaluations)
Product Withdrawal (preceeded by reviews and evaluations)
Changes in Labeling
Work Practice Changes (review for alterations)
Storage and Handling Specifications (review and possible alterations)
Personnel Notifications (review and evaluation)
Liability (statutory, private suits, etc.)
Litigation (over failure to report)

Nonregulatory Requirements. Although regulatory requirements are a visible and strong incentive for carrying out mammalian toxicology, nonregulatory requirements may be more extensive. The latter includes the types of tests and generation of data bases needed by the Surgeon General, for example, to establish standards and criteria for Army personnel not covered by the Occupational Safety and Health Act (OSHA). In addition, the nonregulatory requirements can have as their objectives:

1. To prevent decrements in soldier performance: Decrease in visual acuity, changes in respiratory functions, increase in irritancy, cause of nausea, etc.

2. To reduce the need for or level of disability compensation payments.



SOURCE: Modified EPA Diagram

FIGURE 1 LEGISLATIVE AUTHORITIES AFFECTING MATERIEL LIFE CYCLES

3. To reduce the number of litigations and the size of any settlement associated with personnel having been exposed to toxic substances that affected their health when (a) in the service of the Army or (b) on or near Army installations.

4. To improve the selection of a materiel from a list of alternatives.

The latter helps the materiel developer, Army Materiel Development and Readiness Command (DARCOM), by citing or comparing the relative toxic hazards of alternative materials. Examples of such materials include decontamination chemicals, propellants that result in toxic combustion products, intermediate chemicals used in the manufacture of binary munitions, etc.

Scope of Report

This report reviews and summarizes some of the more important activities completed on the Study. The report has two major and two minor sections. One of the major sections describes the global Army's toxicology requirements. The other major section summarizes a comparative analysis of alternatives for meeting a portion of these requirements. The minor sections include one on special studies completed and one listing what else was done on this portion of the Study, but outside the scope of the final reports.

REQUIREMENTS

An accurate and complete forecast of the Army's toxicology requirements is a mammoth undertaking. It was beyond the three months allotted for the Study. Nevertheless, significant inroads were made using a process of rapid generation of data that simultaneously taps a multitude of highly credible sources.

Scope

The toxicology requirements of the global Army are only a portion of that for the global Department of Defense (DOD). Global refers to every aspect of the Army or DOD business from research through demilitarization of materiel at every location the organization does business or is responsible for business being done.

The global Army's requirements include those that are medically and nonmedically oriented. The former would include the portions that are the responsibility of the Surgeon General, USAMRDC, USAMRDC sub-commands and the Health Services Command (HSC). The nonmedical portion of the requirements include those of the materiel developer (DARCOM), Training and Doctrine Command (TRADOC), etc. Appendix 3 summarizes the major interfaces identified with materiel development requirements, the roles of the Surgeon General and USAMRDC and a simple view of requirements development for a medical activity, chemical defense.

The Army is an integrated conglomerate of many businesses as shown in Table 1. The industrial analogs of these businesses have toxicology testing facilities as does the Army in certain, well established areas such as Army-unique drug/vaccine development. The point is that the Army has a broader need for various types of toxicology than any single industrial company. The Army, in addition to being a materiel developer, is also a distributor, maintainer, user and

TABLE 1 THE ARMY IS AN INTEGRATED CONGLOMERATE OF MANY BUSINESSES

Industry	Private Sector Analog
• Research and Development	Battelle[a]
• Chemicals Development and Manufacturing	Dow Chemical[a]
• Petroleum Products Development	Shell Oil[a]
• Vehicle Development and Manufacturing	General Motors[a]
• Clothing Materiel Development	Burlington
• Transportation (3 Types)	American Airlines[a] Amtrak Railroad Wilson Trucking
• Drug/Vaccine Development	Upjohn[a]
• Medical Devices	Becton Dickenson[a]
• Testing	Underwriters Lab.
• Training	——
• Waste Disposal	——

(a) Have their own toxicology testing facility

disposer of the materiel items it develops. This places the Army in a unique position relative to industrial manufacturers.

Assumptions

A variety of assumptions were used in identifying Army toxicology requirements:

1. All requirements were included when attempting to itemize the global Army's requirements. It should be clearly noted, however, the medical requirements are not involved with offensive chemical warfare developments or their toxicology.

2. A toxicology evaluation completed in the past on a particular type compound reflects, in most cases, a future need for similar testing if a new compound is developed for the same application. A new application for the same compound may require supplemental toxicology. Thus in forecasting toxicology requirements, one should define toxicology work done in the past and extrapolate the same type needs into the future. All projections indicate the scope of the Army's activities are increasing in real dollars over the next four years and possibly the next decade.

3. USAMRDC does not have within its existing facilities the equipment, staff and building for all of the unique toxicology testing fulfilling requirements that the Army should be conducting. If historical toxicology programs remain the norm, adequate facilities exist to do limited types of testing. The assumption of inadequate facilities results, however, because the awareness of needs for testing is increasing. Few, if any, current Army or industrial facilities allow for meeting Army-unique scenarios (see further, Table 6). The belief currently is that the Army contracted volume is less than that which should be carried out given the charter to meeting global Army needs and adequate financial support to meet them, etc.

4. Equipment, facilities and testing protocols do not exist elsewhere to meet the Army's toxicology testing requirements.

5. The available facilities at other government organizations (EPA, NIOSH, etc.) are subject to being inaccessible for Army studies because:
   a. That organization's needs take priority.
   b. In case of manpower cuts or reductions in force (RIF) they are apt to be taken in areas that are not critical to the parent organization.

Clarifiers

Various issues must be reviewed to clarify the information discussed in the remainder of the report.

Uniqueness of Toxicology Requirements

Several things make toxicology requirements more unique than other requirements:

1. The time required for toxicology testing cannot be shortened by adding more money or people for a specific test.

2. The time is long (approximately three to five years) and the cost is high (approximately three to five million dollars) to develop a comprehensive data base for regulatory compliance of a chemical. For example the seven phases identified below give an indication of the actual time needed to do a comprehensive rodent chemical carcinogenesis experiment. When the sequential stages are combined each chemical takes an average 64 months to complete; that is, after a chemical has been found to need testing.

Phases	Stage of Experiment	Months
I	Pretesting	15
II	Acute, 14 day, and 90 day studies	11
III	Chronic bioassay	25
IV	Draft Report Preparation	3
V	Internal Peer-Review	6
VI	External Peer-Review	2
VII	Report Issuance	2

(U.S. Department of Health and Human Services 1980c).

3. Decisions on the acceptability of the Army's data base and its interpretation as a standard is outside the control of the Army for regulatory requirements. Further, the judgment of the acceptability of the data base is made only after the data has been generated and submitted.

4. Toxicology does not solve crises after they occur. It clarifies the extent of the "crisis" and provides data/information to hopefully preclude future "crises"[(a)].

What Was Not Covered

The Contract's Statement of Work, at the direction of the Army, focused on applied mammalian toxicology research/testing but did not include:

1. Basic toxicology research.

2. Training of personnel in toxicology.

3. Aspects and scope of the occupational health/health hazard assessment programs other than toxicology. The mammalian toxicology testing, however, will furnish information for decision-making on occupational and environmental health programs.

(a) A toxicology related crisis only draws attention to what shouldn't have been not what should be done.

4. Environmental toxicology health effects to determine effects of pollutants on animals other than humans such as aquatic organisms, plant life, etc.

5. Epidemiology.

6. Full-service toxicology capability.

Within the area of applied toxicology, the Army's specified that the following types of requirements not be considered in the Study:

1. Toxicology requirements associated with drugs and vaccines developments.

2. Toxicology associated with offensive chemical warfare (USAMRDC has no involvement with this technology).

3. Toxicology associated with defensive biological warfare.

4. Toxicology associated with nuclear warfare.

Basic Toxicology Research. Although, outside of the Study's scope, the requirements associated with basic toxicology research were itemized in the list of identified requirements (Life Systems, Inc. 1981c).

Training. Toxicology training is a very important mission. Toxicology related personnel will be in short supply for the next decade (Development Planning and Research Associates, Inc. and ICF, Inc. 1980, ICF, Inc. 1980). An Army training program would be a cost-effective method for meeting the Army's toxicology needs of the future.

Toxicology in Occupational Health or Health Hazard Assessment Programs. Toxicology is a subset of Occupational Health, which is a subset of Health Hazard Assessment. Toxicology is one aspect of Health Hazard Assessment (HHA). It is a program recommendation that the portion of the Army's toxicology requirements that fall under HHA should be included as part of a HHA program rather than incorporated into an added toxicology Facility capability.

Environmental Health Effects. The nature of environmental effects can be roughly compared to those that occur in human toxicology, immediate or acute effects and those that occur with longer term lower level exposures, analogous to chronic effects. Table 2 summarizes the direct and indirect environmental effect of chemicals. This important area was outside the Study's scope. Thus, on the Study, the term "toxicology" refers to mammalian toxicology targeted at determining human health effects, as opposed to effects on aquatic organisms, plants or wildlife.

Epidemiology. Although there is growing advocacy for employing epidemiological techniques in human health effects investigations and we will probably see increasing focus on the use of epidemiology in the future, it is not included as part of the Army's toxicology requirements.

TABLE 2 DIRECT AND INDIRECT ENVIRONMENTAL EFFECTS OF CHEMICALS

Areas Affected	Potential Effects
Species	Toxicology
Aquatic species	Lethality
Terrestrial species	Availability
Avian species	Propogation
Man—by ingestion or based on availability	Growth
Plant life	Availability
Media	Odor
Air	Color
Water	Utility
Soil	Nutrition
	Aesthetics
	Health (to man and other species)
Ecosystems	Disruptions based on or involving
Species and Media Interrelationships	any or all of the above
Artifacts	Corrosion
Buildings	Discoloration
Personal Property	Durability
Public Property	Aesthetics

Source: Domiquez 1979, p. 112.

Differentiating Levels of Toxicology Capability

At least six levels of toxicology capability were formulated. They are summarized in Table 3 along with the type of service provided. They range from production type toxicology testing to full service mammalian toxicology. The latter includes all the levels and all scientific disciplines within toxicology. Besides general toxicology, these include behavioral, metabolism/pharmacokinetics, pharmacodynamics, oncogenic, respiratory physiology, reproduction, teratology and neurotoxicology.

Full Service Capability Terminology

As used on the current Study the expression full service capability was divided into four areas:

1. Service up to the point of determining the testing actually needed.

2. Toxicology testing of either the production type or the applied research type.

3. Service carried out in parallel with the testing (some series of tests take three or more years to be completed).

4. Service after testing results are interpreted.

In all of the four areas the expression full service includes all toxicology disciplines (e.g., oncology, teratology, etc.)

A more complete description of the tasks provided by a full service capability is contained in Appendix 4 and, for services that could be provided on each individual toxicology project assignment, in Appendix 5. These lists are not meant to be all encompassing or necessarily listed in order of occurrence. They do provide an insight, however, to the many other aspects of toxicology besides testing.

Full Service Toxicology Tasks

The Army needs full service toxicology which includes:

1. Alerting the appropriate DA agency to potential toxic hazards - a requirement identification responsiblity.

2. Literature reviews, evaluations of manufacturing processes, weapons environments, etc. to determine if testing is needed and the priority for testing.

3. Monitoring to ascertain compliance to criteria or standards.

4. Maintaining data bases resulting from toxicology programs.

Full Service Tasks Vary with Time

Figure 2 presents schematically how the full services tasks vary as a function of time. The identification of a global Army requirement can occur before

TABLE 3 LEVELS OF TOXICOLOGY CAPABILITY

Level of Capability	Type of Service
• Mammalian Toxicology Testing	Using standard protocols
• Applied Mammalian Toxicology Research	Includes methodology and protocol development
• Limited Service Mammalian Toxicology Capability[a]	Includes consulting and activities before, during and after testing programs
• Basic Mammalian Toxicology Research	Includes reducing cost of future testing and developing better extrapolations (e.g., animals-to-man)
• Personnel Training in Army Mammalian Toxicology Technology	Includes providing continuous "smart buyer" capability, continuity of historical effort, needed inspectors
• Full Service Mammalian Toxicology Capability[a]	Includes all scientific disciplines (general to behavioral, neuro-toxicology, oncogenic, etc.)

(a) Testing and applied research

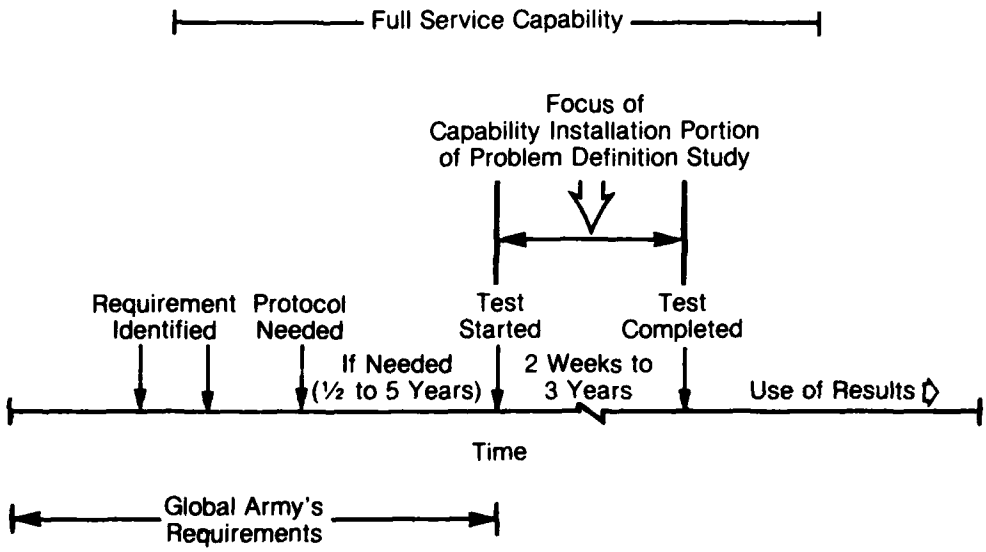


FIGURE 2 FULL SERVICE TASKS VARY OVER TIME

toxicology related personnel are involved up to the time testing is first requested. Thus, requirements can be identified outside or within the toxicology framework. An example of an early toxicology task is determining if a special protocol is required.

As shown in Figure 2, the scope of the capability or Facility Installation portion of the Study was associated with the timeframe between test start and test completion. A time span that could typically be two weeks to three years.

Complexity of the Study

The Study was complex in that parts of four different Studies existed in this one Study. As noted, the focus was on global Army requirements, including medical and nonmedical requirements, met and unmet. The medical requirements are being met in part by USAMRDC. The USAMRDC capability exists primarily at four laboratories (USAMRICD, USAMBRDL, WRAIR and LAIR) doing or involved with toxicology. No clear description of the capability and capacity of each laboratory, however, exists. Further, that portion of the requirements to be considered during the comparative analysis and to be considered in the conceptual design of an added capability (Facility) were different and represented only a portion of the total medical requirements.

The USAMRDC portion of global Army requirements is unclear because of the uncertainty in boundaries of responsibilities between various Army agencies within the Department of the Army (DA) and the impact on USAMRDC from the enactment of recent laws, e.g., TSCA, the Resource Conservation and Recovery Act (RCRA), etc.

Many Questions are Unanswered

1. How many new items are introduced into the RDT&E system annually? Difficult but not impossible to determine.

2. What systems are classified as major systems, minor systems and other materiel? The program identified 53 major systems (defined as those with Program Managers), anticipated there might be 1,000 minor systems and more than 10,000 other applicable inventoried items.

3. What documents list and describe items already in inventory (not identifiable by RDT&E documents or the procurements budgets) that, with proper screening, would identify potential toxicology requirements?

Other questions include date of first issue or projected date of issue, date of first buy or projected date of first buy, description of materiel, point of contact, crew size and passenger load if its a vehicle, funding level status (6.1, 6.2, 6.3, 6.4), total budget for the development, date needed, etc. These were not answered during the Study.

Requirements Being Met and New Requirements

Following identification of global Army requirements, they must be segregated into requirements that are:

1. Being met because current requirements have been part of the normal way of doing Army business for many years (e.g., the toxicology associated with drug and vaccine developments).

2. Starting to be met but are not yet recognized broadly throughout the Army requirements.

3. Just starting to be recognized as a result of an awareness of the implication of pollution laws.

Table 4 segregates the 16 different toxicology related regulations into the three categories noted above.

A final category of requirements is where the toxicology is but a portion of larger requirements -- an occupational health or HHA program. In this case, the requirements for toxicology should be grouped as part of the occupational health or HHA program and not carried out and implemented independent of the other parts to these programs.

Requirement Uncertainties

The Study took a significant step toward formulating the Army's toxicology requirements. Because of Study constraints (Appendix 6), however, additional effort is needed to more clearly identify the specific toxicology tests to be carried out, who has specific responsibility for these tests, who will provide the resources, which tests are part of typical development processes and inherent in existing budget requests, which portions are part of the broader requirements of occupational health or health hazard assessment and which are truly unmet, medical requirements that cannot effectively be met utilizing existing approaches to meeting the Army's needs.

Risk/Benefit Analysis

Risk/benefit analyses must be used in screening potential requirements as part of a process of forecasting future requirements. This capability which does not involve testing should be added to the Army's capability in toxicology. The balance between risk, hazard, cost and benefit is an art and technology of itself not included in the Study.

Type of Toxicology

In identifying the Army's toxicology requirements three categories of tests were identified:

1. General Toxicology Tests.
2. Special Scientific Toxicology Tests (Studies).[a]
3. Genetic Toxicology Tests.

Appendix 7 presents a discussion of these tests.

(a) For the remainder of the report, special scientific toxicology tests will be referred to as studies not tests. This is done to reflect the research orientation of these activities.

TABLE 4 IMPACT OF CURRENT REGULATIONS ON REQUIREMENTS

Been Handled In Past	Recognized Implementation Underway	New Implementation Needed
AEA	CAA	OSHA — Army's Civilians
AWA	CWA	"OSHA" — Soldiers[a]
CPSA	FHSA	RCRA
FFDCA	FIFRA	TSCA
HMTA	SDWA	
NEPA		
OSHA		
PHSA		

(a) Non-regulatory requirements

There is considerable uncertainty in the actual volume of toxicology work because of the options available concerning tests. This impacts the resources needed to meet the Army's requirements. Additional uncertainty is associated with when to test and who should commit to testing, USAMRDC, Medical Bioengineering Research and Development Laboratory (USAMBRDL) or Army Environmental Hygiene Agency (AEHA). As expected, some requirements will be clear cut, other uncertain. But, once a pattern is established, the degree of uncertainty will wane.

Facility Means Selected Facility

The actual capability and capacity included in any added USAMRDC new facility (new meaning newly built or a renovated site) remains to be determined and is an USAMRDC/DA decision. In the Study reports, the term Facility almost universally refers to the facility resulting from the selected capability and capacity. The Facility can be a full service, limited service or full service but with only certain toxicology research capabilities incorporated.

Existing Requirements Identification Procedures

The current approaches for identification of Army toxicology requirements are informal, incomplete and nonsystematic. They are extensive, however, in that they include all of the following to some unstructured degree:

1. A request from a program manager or developer.
2. A complaint from a user (e.g., military unit, division commander).
3. Medical referrals.
4. Review of requirements documents on a when-time-is-available basis.
5. Participation at In-Process Reviews (IPRs).
6. Results from industrial hygiene surveys.
7. Informed of regulatory mandates.
8. Actions by local, state or federal government agencies.
9. Actions of public interest group or press/media.
10. Actions by courts.
11. Requests by a manufacturer that is also a government contractor.
12. Results from an installation environmental survey (water, air or solid waste).
13. Request from a troop or installation commander.

Although the list of existing methods for identifying requirements is long, the "organization" into which these requests are made is not well defined and does not exist as a central function on an organization chart. Also, individuals to whom requests are placed are typically not chartered or funded to respond systematically to the requests.

Sources Used

A variety of techniques were initiated simultaneously to scope the Army's toxicology requirements. They included the following:

1. A review of the DA budget for the fiscal years 1979 through 1981 (House of Representatives, 96th Congress 1980b).

2. A review of the DA procurement budget for the four years 1979 through 1982 (DMS, Inc. 1980a). This identified the types of material being procured (as opposed to being in the RDT&E stage of the inventory). From this the requirements categories used throughout the remainder of the Study were selected including:

    a. Aircraft.
    b. Missiles.
    c. Weapons and Tactical Combat Vehicles.
    d. Ammunition.
    e. Others.

3. A review of the DA RDT&E budget for the four fiscal years 1979 through 1982 (DMS, Inc. 1980b). There are two major divisions:

    a. Budget activity:

        1. Technology Base.
        2. Advance Technology Development.
        3. Strategic Weapons.
        4. Tactical Programs.
        5. Intelligence and Communications.
        6. Defense-wide Mission Support.

    b. R&D categories:

        1. 6.1 Research.
        2. 6.2 Exploratory Development.
        3. 6.3 Advanced Development.
        4. 6.4 Engineering Development.
        5. 6.5 Management and Support.
        6. 6.6 Operational Systems Development.

    The titles of each of the program elements in the R&D categories 6.1 through 6.6 were evaluated for potential toxicology requirements. The Study's constraints, however, did not allow investigating the backup material on each of the identified potential toxicology related programs within the R&D categories.

4. A review of the 19 areas of the Catalog of Approved Requirements Documents (CARDS).

5. A review of documents involving USAMRDC efforts. Included were:

    a. A "Report of Mammalian Toxicology Testing Requirements and Concepts for Solution" by R. H. Reuter, dated 1979, USAMBRDL. This report itemized requirements for five different USAMRDC mission areas, according to three categories and an assigned priority.

    b. Three sections of the USAMRDC "Long Range Plans," mission areas 1, 3 and 4.

c. A report entitled "Management Plan for Occupational Health Criteria Research Program of USAMBRDL" written by R. Shiotsuka, dated 1979.

d. The scope of past and current USAMRDC programs as reflected on Form 1498s, Research and Technology Work Summary.

6. A review of the Army Weapon Systems Booklet (U.S. Department of Army 1980) that serves as an unclassified reference on selected major Army weapons and equipment.

7. A review of the recent Description of the Army's RT&E weaponry (Ludvigsen 1980).

8. A screening of many isolated documents, such as the Army RD&A magazine, to identify the new developments. This identified such requirements as those associated with the synthetic fuels program, many of the chemical protective and decontamination equipment developments, chemical demilitarization and installation restoration requirements from the Army Toxic and Hazardous Materials Agency.

9. A review of the toxicology being done by:

   a. USAMBRDL (the Form 1498s), no other data was provided.
   b. CSL.
   c. AEHA.(a)

   The latter was done through a review of the Annual Historical Report of AMEDD Activities, US AEHA, for the periods 1975 through 1979. These were very helpful in defining past examples of needed toxicology testing.

10. Various reports containing information on specific chemicals and their relationship to Army requirements (Barbeito 1979, Brown et al. 1977, Brown et al. 1978, Christ 1979, Frost and Sullivan, Inc. 1980, Procurement Associates, Inc. 1980).

Because of the three months time frame, only the documents readily available could be obtained and evaluated. Additional requests were made for more detailed data when identified. Some are still being received. They will be incorporated into the requirements data base or report (Life Systems, Inc. 1981c).

(a) The AEHA had the best method of yearly reporting what it did in toxicology (U.S. Army Environmental Health Agency 1979). It covers number of reports prepared, draft criteria documents reviewed, medical reviews made, literature surveys, protocols reviewed, studies requested, studies active and work units. It appears to be doing an exceptional job in meeting many Army toxicology requirements (particularly before testing requirements) from a range of Army users.

Many Ways to View Requirements

Various ways exist for viewing the Army's requirements. These include:

1. According to the compounds involved, the applications/uses for the compounds and the effects resulting from materiel use. Table 5 illustrates this method.

2. According to categories:

   a. A category including toxicology that has been done for many years (e.g., drug developments (FFDCA laws)).

   b. A category including toxicology that is a part of HHA Program.

   c. A category including basic toxicology research.

   d. A category including toxicology that is not being met and futher divided into medical and nonmedical.

   e. A category including toxicology associated with laws and further divided into TSCA, RCRA, FIFRA, OSHA, HMTA, etc.

3. According to a three dimensional view or data base.

The latter approach is considered most complete. It is the approach recommended the Army follow in its continuing quest for identifying toxicology so as to avoid legal entanglements and provide an environment of minimum hazard for its personnel.

Three Dimensions of Requirements

The global Army's requirements have at least three dimensions:

1. The materiel requirement itself: chemical, chemical use, weapons creating an environment and manufacturing plant.

2. The requirements for a given materiel as they change over the life cycle of a materiel (e.g., chemical).

3. The specific toxicology service (task) requirements involved, of which only one portion is associated with testing.

This three dimensional block, for all the Army's materiel (past, present and 10-year future) is enormous.

Figure 3 pictorially represents the three dimensional scope of the toxicology requirements. (It could readily be expanded to include consideration of environmental toxicology by minor modifications in the axis entitled "Toxicology Tasks". This is desirable to save the cost of re-inventing the wheel and doing these requirements independently.

TABLE 5 ANOTHER WAY TO VIEW REQUIREMENTS

Compounds

- Single Chemicals (Vapors, Aerosols, Particulates)
- Multiple Chemicals (Synergisms, Antagonisms, Additives)
- Foreign Supplied (Materiel)
- Categories (Industrial Chemicals, Industrial Processes, Industrial By-products, Pharmaceuticals, etc.)
- Chemical Life Cycle

Applications/Uses

- Environments (Resulting from Use)
  - Combat — Chemical Warfare
  - Combat — Smokes & Obscurants
- Reaction Products (e.g., Exhausts) — Screen for Reaction — and By-Products
- Landlord (Demilitarization)
- Data Base Generation
- Assessment, Prevention, Diagnosis, Monitoring
- Research Laboratory

Effects

- On Operators (Army as Employer)
- Of Risk/Benefit Analyses (Vol. Chemical, Hazard, ...)
- On Behavior
- Short Term/Long Term
- Of Plans, Programs & Priorities (e.g., DARDOM, USAMRDC, etc.)

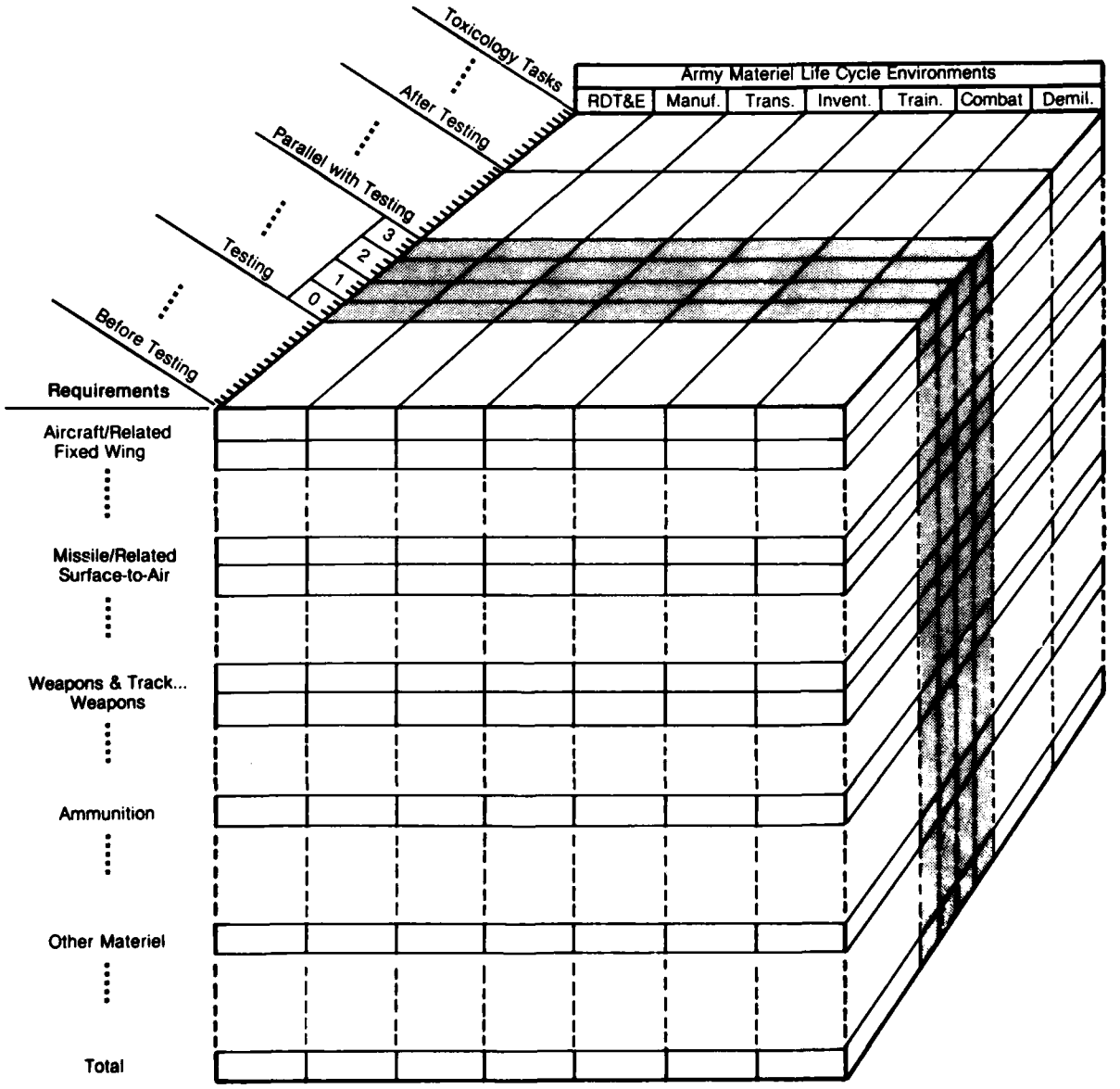


FIGURE 3 REQUIREMENTS VOLUME

Requirement Identification

The requirements (vertical axis) are summarized in a report entitled, "Global Army Toxicology Requirements" (Life Systems, Inc. 1981c). It is not included as part of this report because of its size (over 30 pages at the 9th level). Each of these requirements should now be evaluated to determine:

1. Is toxicology involved?
2. If so, is it regulatory or nonregulatory?
3. If regulatory, which law, executive order, etc.?
4. Is it medical or nonmedical?
5. If medical, is it a USAMRDC or HSC responsibility?
6. Is the toxicology or the materiel development funded and with what source (e.g., 6.1, 6.2, 6.3 or 6.4 level)?
7. What type toxicology tasks are needed:
    a. Before testing?
    b. Testing?
    c. If testing, Tier 0, 1, 2, 3?
    d. Parallel with testing?
    e. After testing?
8. What is the priority?
    a. Is it holding up materiel fielding?
    b. Could it hold up material fielding?
    c. When would the hazard impact?
        i. Immediate?
        ii. Long term?
9. When should testing be undertaken?
10. How long will testing take and how much will it cost?
11. What form should be tested -- reagent grade, commercial grade, etc.?

Extensive as these questions may be, they are only representative of those that the Army's toxicology effort must answer.

Requirements categories such as Aircraft, Missiles and Weapons and Track Combat Vehicles often have toxicology requirements because of the environment the weapon generates. The Ammunition category often has requirements based upon the chemical involved and the environments in and around the plants that manufacture the ammunitions. The category called Other Materiel has the broadest types of requirements: toxicology resulting from the chemical itself, its use, the environment created from its use, the impact upon the terrestrial environment (land, water and air), etc.

Special Consideration for Army-Unique

Of particular importance to the Study were the Army-unique requirements. An example of an Army-unique exposure scenario is presented in Table 6. The exposure conditions are characterized by short-term, repeated exposure at intense concentrations. Often these exposures occur with concomitant exposure

TABLE 6 ARMY-UNIQUE EXPOSURE SCENARIO

Characteristic	Level
Short Term Exposure	<1 min to 1 hr
Repeated Exposure	1 to 60 times/10 hr day
Intermittent Exposure Frequencies	1 day/week to >90 days continuous
Intense Concentration	Above existing ceilings
Unique Environmental Conditions	
Temperature	– 40 to 140 F
Relative Humidity	>10 to 100%
Ambient Pressure	Sea Level to that at 8,000 ft
Associated Stress Conditions	
Noise	Loud, Sporadic
Vibration	Constant, but Varying
Shock	Periodic, Intense
Overpressures	Blasts, Shock Waves
Psychological	Stress, Threats

conditions. These concomitant exposures include exposure to other chemicals and to ranges in temperature, noise pressure, vibration, etc. the soldier is expected to perform under. Table 7 briefly itemizes these concomitant exposures.

Multiple Techniques Must be Used

The methodology the Study followed in identifying requirements resulted in identifying 13 approaches. Each will identify certain specific requirements, but will also miss others. Each has a different cost in terms of dollars and time. Table 8 lists the 13 approaches, what will be identified and missed and the estimated price and time required to use that approach.

Top Down

The top down is an essential approach. It is systematic and ties the requirements back to the manner in which RDT&E and procurement budgets are formulated and approved. Of course, it will miss the requirements from situations already in the inventory, the existing manufacturing plants, the training environments, etc. To fully implement the technique will take a long time and a medium amount of money. A low, medium and high cost is defined as less than one-person year, one-person to less than ten-person years and greater than ten-person years, respectively. A short, medium and long time is defined as less than six months, six months to 18 months and more than 18 months, respectively. This approach was initiated but not fully used.

Table 9 illustrates levels 1 and 2 for the five categories of the global Army requirements. The Study showed that the top down approach does not identify a specific toxicology requirement until at least the fourth and sometimes not until the tenth level depending upon the particular category.

Figure 4 illustrates how, with the top down approach, one may have to reach level 9 before the specific toxicology project becomes identified. (See left-hand side of triangle.)

Bottom Up

The bottom up technique is the most thorough approach. It will miss little. It tends to be nonsystematic, complex. The requirements identifier would tend to become lost. The time would be long and the cost would be high (greater than 10 people-years). The technique was not used on the Study.

Spot Sampling

Spot sampling was one of the approaches used on the current program. Its value was rapid identification of specific toxicology testing needs. Most of the other techniques were not able to do this within the Study's time constraints.

Random Sampling

This is a formalized method of sampling. The greater the number of samples taken, the greater the percentage of the requirements identified. It was not used. It is not recommended for future use because the number and type of requirements are not uniformly distributed among the Army's materiel.

TABLE 7 CONCOMITANT EXPOSURES THAT WILL MODIFY STANDARD TOXICOLOGY TESTS

Temperature	Hot / Cold
Noise	Loud / Nonauditory, Intermittent and Continuous
Vibration	Continuous, Peaks
Shock	Periodic, Intense
G-Forces	None / ??
Overpressures	Blasts, Shock Waves
Relative Humidity	Dry / Wet
Visibility	Light / Dark; Fog / Rain / Snow
Ambient Pressures	Mountain/Sea Level
Psychological State	Stressful (Threatening, Uncertain), Neuropsychiatric
Radiation	Ionizing / Nonionizing

TABLE 8 ONE TECHNIQUE WILL NEVER IDENTIFY ALL THE REQUIREMENTS. TO DO IT THOROUGHLY REQUIRES MANY APPROACHES

No.	Approach	What Will Identify?	What Will Miss?	Price	
				Cost?	Time?
1	Top Down	RDT&E and Procurement	Inventory, Existing Plants	Med.	Long
2	Bottom Up	Specific Cases	Little	High	Long
3	Spot Sampling	Specific Cases	Most	Low	Short
4	Random Sampling	Percentage	Percentage	Med.	Med.
5	Talking to PMs	50 Majors	1000's Minor, Uses	Low	Med.
6	Life Cycle Segmenting	Less Obvious	Little	High	Long
7	Legalistic	Regulator	Non-regulator, What's in lab.	Med.	Med.
8	Manufacturing Process Review	Starting, Intermediate Final & By-Products	Applications, Uses	Med.	Med.
9	More of Same (Testing)	Nothing New	New Needs, Unexpected	Low	Low
10	Squeaking Wheel	One Probable	All Others	Low	Short
11	Forecasting Changes	New Issues	Existing Issues	Med.	Low
12	Questionnaires	Known & Some Unknowns	Hard to Find	Low	Med.
13	Life Cycle Network	New Materiel	Inventory	Med.	Long

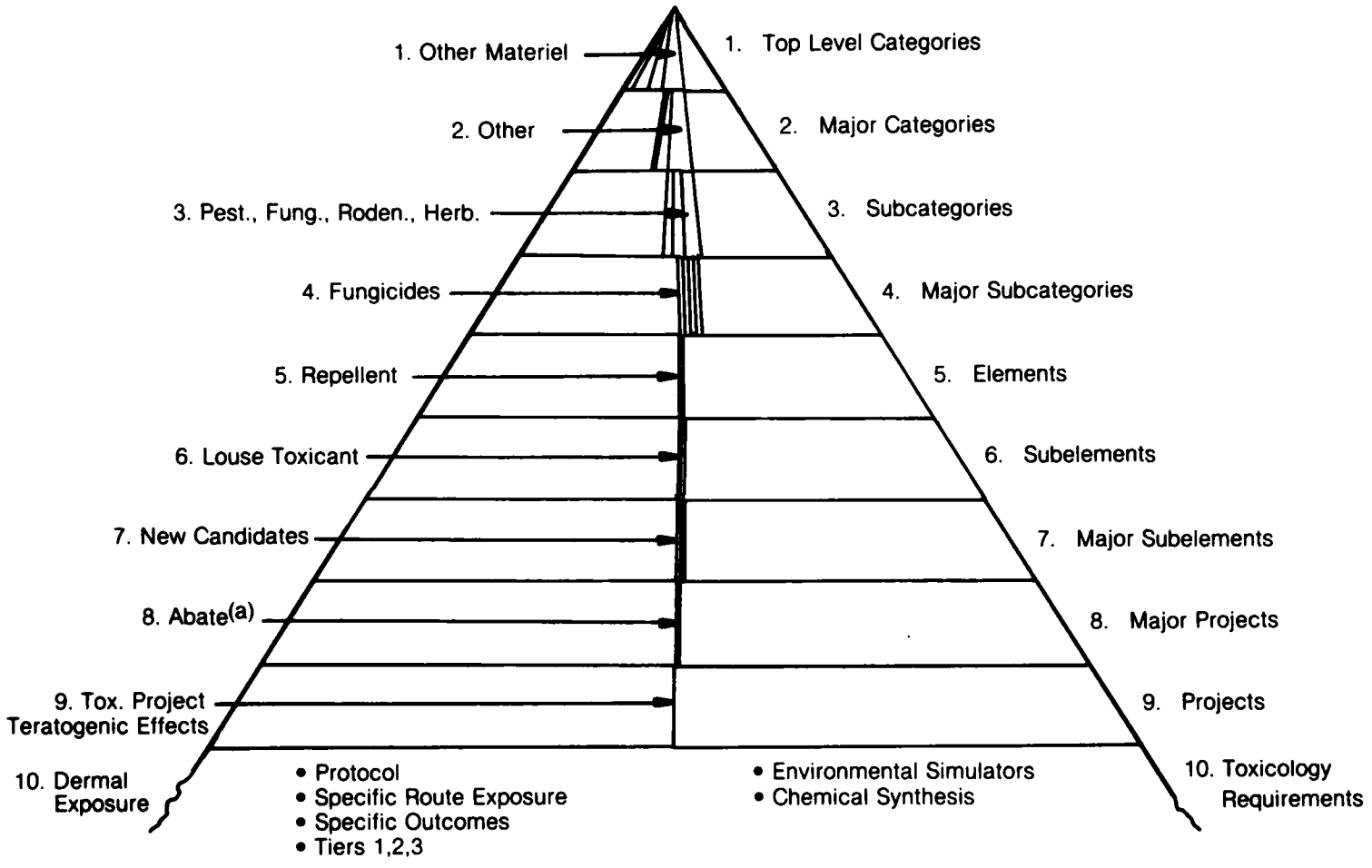
TABLE 9 GLOBAL ARMY REQUIREMENTS CATEGORIES

Level 1

- Aircraft (& Related Equipment)
- Missiles (& Related Equipment)
- Weapons and Tracked Combat Vehicles (& Related Equipment)
- Ammunition (& Related Materiel)
- Other Materiel

Level 2

- Aircraft (& Related Equipment)
  - Fixed Wing
  - Helicopter
  - Technology Base
- Missiles (& Related Equipment)
  - Surface-to-Air
  - Air-to-Surface
  - Surface-to-Surface
  - Antitank/Assault
  - Technology Base
- Weapons and Tracked Combat Vehicles (& Related Equipment)
  - Weapons
  - Tracked Combat Vehicles
  - Technology Base
- Ammunition (& Related Materiel)
  - Ammunition
  - Technology Base
  - Ammunition Production Base Support
- Other Materiel
  - Tactical & Support Vehicles
  - Communications & Electronics
  - Other



(a) 0,0,0,",-Tetramethyl-0-0"-thio-di-p-phenylene phosphorothioate

FIGURE 4 CROSS SECTION OF REQUIREMENTS "MINE"

Talking to the DARCOM Program Managers

There are 53 major weapon/materiel systems identified within DARCOM. An interview with the responsible person within a particular Program Manager's staff should result in identification of potential toxicology requirements for the major weapon/materiel. It has the advantage of addressing the high priority and high cost materiel development programs of the Army. It misses, however, many of the minor programs where the Army's more critical toxicology vulnerabilities may exist.

Table 10 presents a list of the DARCOM major programs and their Program Managers coded to reflect those likely to have toxicology requirements.

Life Cycle Segmenting

This is a very important technique. It looks at each of the requirements during each of the life cycle categories. Table 11 presents the major life cycle categories. Many current unmet toxicology requirements exist in the first four categories of the life cycle. This is because the materiel was manufactured and procured at a time when the hazards, for example, of chemical substances, were not appreciated. Requirements in the latter life cycle stages represent a bow wave of requirements that exist now but will decrease with time. Judgments have to be made, therefore, to determine which of these "existing" conditions should be corrected and which will disappear through attrition of the materiel.

The goal of the life cycle segmenting approach is to identify the toxicology needs during the RDT&E phase, especially the 6.2 phase. This will avoid costly re-engineering, removal of the material from inventory, etc. The materiel currently being funded with 6.3 and 6.4 level monies represent priority requirements since these materiel are very close to the procurement stage. Correcting problems in fielded materiel is expensive and represents a failure of management.

The Army actually divides the life cycle slightly different than reflected in Table 11 (U.S. Department of the Army 1977b).

Category	Network Code
Conceptual	100
Validation	200 and 300
Full Scale Development	400 and 500
Production	600 and 700
Operational	800
Disposal	900

The Study selected the alternative as a temporary measure to provide a better match between portions of the life cycle and the applicability of different types of laws or requirements.

Legalistic

This approach should be used. It asks the Army Judge Advocate to interpret the laws and determine the type, format and amount of data needed to conform

TABLE 10 DARCOM MAJOR PROGRAMS/PROGRAM MANAGERS ASSOCIATED WITH AMTR/T

Acronyms	Description	Program Manager	Projected Mammalian Toxicology Services[b]	Chemical		Environment		
				Specific	Uses	Weapon	Plant	Health
AAH	Advanced Attack Helicopter	MG Browne	S			X		
ACVT	Armored Combat Vehicle Technology	LTC Welch	S			X		
ADCCS	Air Defense Command Control System	COL Wyatt	-					
ADTDS	Air Defense Tactical Data Systems	---	-					
ASE	Aircraft Survivability Equipment	COL DeLany	M	X	X	X		
ASH	Advanced Scout Helicopter	COL Rundgren	S			X		
ATACS	Army Tactical Communication Systems	COL Rhodes	-					
ATD	Armor Training Division	LTC Meeth	-			X		X
CAC	Control and Analysis Centers	COL Irish	S					
CAWS	Cannon Artillery Weapons Systems	COL Pointer	M			X		
CE	Commercial Construction & Selected Material Handling Equipment	LTC Vachon	-					
CHAP/FAAR	Chaparral/Forward Area Alert Radar	COL Stubbs	S			X		
DCSCS-DCS	(Army) Communications Systems	MG Lasher	-					
DIVAD	Division Air Defense Gun	COL Adsit	S			X		
FAMACE/UET	Family of Military Engineer Construction Equipment/Universal Engineer Tractor	COL Benfer	-					
FIREFINDER/ REMBASS	Firefinder/Remotely Monitored Battlefield Sensor System	COL Chesbro	-					
FVA	Fighting Vehicle Armament	COL Sowers	S			X		
FVS	Fighting Vehicle Systems	BG Whalen	S			X		
HELLFIRE/GLD	Heliborne Laser Fire & Forget Missile Systems/Ground Laser Designators	COL Cass	-					
HET	Heavy Equipment Transporter	LTC Charbonneau	-					
ITV	Improved TOW Vehicle	COL Chernault	S			X		
MEP	Mobile Electric Power	COL Rowe	-					
MLRS	Multiple Launch Rocket System	COL Hatchett	S			X		
MSCS	Multi-Service Communications Sys.	COL Callahan	-					
NAVCON	Navigation Control Systems	COL White	-					
NUCMUN	Nuclear Munitions	COL Farmer	S			X		X
PLRS/TIDS	Position Location Reporting System Tactical Information Distribution Systems	COL Morgan	-					
RPV	Remotely Piloted Vehicle	COL Christensen	-					
SANG	Saudi Arabian National Modernization Program	BG Bartlett	S	X	X	X		X
SEMA	Special Electronic Mission Aircraft	COL Berdux	S			X		
SINCGARS	Single Chanel Ground & Airborne Radio Subsystem	COL Wilkins	-					
SOTAS	Stand-Off Target Acquisition/Attack Systems	COL Davis	S			X		
TACFIRE/ FATDS	Tactical Fire Direction System/ Tactical Information Distribution Systems	COL Luck	-					
TADS/PNVS	Target Acquisition Designation System/Pilot Night Vision System	COL Wray	-					
TMAS	Tank Main Armament System	COL Appling	M			X		
TMDS	Test Measurement & Diagnostic	LTC Marangola	-					
TOS/OITDS	Tactical Operations System/Operation & Intelligence Tactical Data Systems	COL Salisbury	-					
TRADE	Training Devices	COL Campbell	M			X		X
COBRA	Attack Helicopter	COL Williamson	S			X		
SMOKE	Smoke & Obscurant	COL Eure	L	X	X	X	X	X
STINGER	Portable Antiaircraft Missile	COL Rambo	S			X		
PATRIOT	Surface-to-Air Missile	MG Street	S			X		
TOW/DRAGON	Antitank Missile	COL Williamson	S			X		
HAWK	Air Defense Missile	COL Stevens	S			X		
BLACKHAWK	Helicopter	COL Anderson	S			X		
PERSHING	Support Missile	COL Fiorentino	S			X		
VIPER	Battlefield Light Antitank Missile	COL Larkins	S			X		
SATCOM	Satellite Communications	COL Lindberg	-					
M60 TANKS	Main Battle Tank	COL Bayruns	S			X		
M113	Armored Personnel Casualty	LTC J. Logan	S			X		
30MM	Ammunition	LTD D. Logan	S	X	X	X	X	X
CH-47M	Helicopter	COL Gordy	-					
XM1 TANK	Main Battle Tank	MG Ball	S			X		

(a) Requirement relative to RDT&E phases only.
(b) Code letters:
Small - Estimate one requirement (environment, chemical, location or time) with cost $1 million ± 50%;
Medium - Estimate 2-3 requirements with cost $3 million ± 50%; and
Large - Estimate more than 3 requirements with cost of $9 million ± 50%.

TABLE 11 GLOBAL ARMY'S BUSINESS ENVIRONMENTS WHICH REQUIRE TOXICOLOGY TECHNOLOGY[a]

1. RDT & E
2. Manufacturing
3. Transporting
4. Inventory
   a. In use
   b. Depot (Storage, Maintenance)
5. Training
6. Combat Operations
7. Demilitarization (Deactivation, Disposal)

(a) This environment includes military and civilian personnel and civilians working in or living around Army business activities.

to the laws. It can also alert the DA to the areas where most problems will occur. The program did not provide for interviews with the Army Judge Advocate. An awareness of the interpretation, and the Army's responsibility to conform to regulations, will identify many, if not most, regulatory requirements.

Manufacturing Process Review

This approach will find the requirements based on chemicals that are part of the manufacturing process including:

1. Starting chemicals.
2. Intermediate chemicals.
3. Final chemicals.
4. Byproduct chemicals.

The approach includes evaluation of the environmental health factors (air, water and land pollution) that are possible. The final chemical should also be evaluated on the basis of exposures associated with its various projected uses.

More of the Same

This approach was used. It does not greatly expand what is already known. It misses new needs and the unexpected areas of vulnerability. It can be used to forecast by extrapolating from the past.

Squeaking Wheel

This approach was not used since no squeaks were heard. The Study's objective, however, was not to identify those complaining about a problem but to systematically identify requirements and methods for requirements identification.

Forecasting Changes

This technique was used to a limited extent as part of the third thrust of the Study, the impact of future changes in regulatory and toxicology technology as they impact requirements. The results of these activities are summarized elsewhere (Life Systems, Inc. 1981b).

Questionnaires

This approach was not utilized. It should be an important one. It requires, however, the preparation of a questionnaire to assist nontoxicology related people in identifying their toxicology requirements. It would provide one of the faster methods for obtaining information at a relatively low cost. The upfront funding for a good questionnaire is needed.

Life Cycle Network

This is an essential method for best providing service to the materiel developer (DARCOM). Appendix 8 identifies the two locations within DARCOM's life cycle management process where health hazard assessment (of which toxicology is a subset) interfaces the development cycle and where inputs are possible (U.S.

Department of the Army 1977b). These occur at network blocks 158 and 318. Various other documents needed at various network blocks could require, input or discuss toxicology of the materiel. The Critical Issues document, for example, could provide a toxicology input into the cycle at network blocks 126 and 467 (see Appendix 8).

Figure 5 shows the various regulations that, in general, impact the materiel during each of the major life cycle categories.

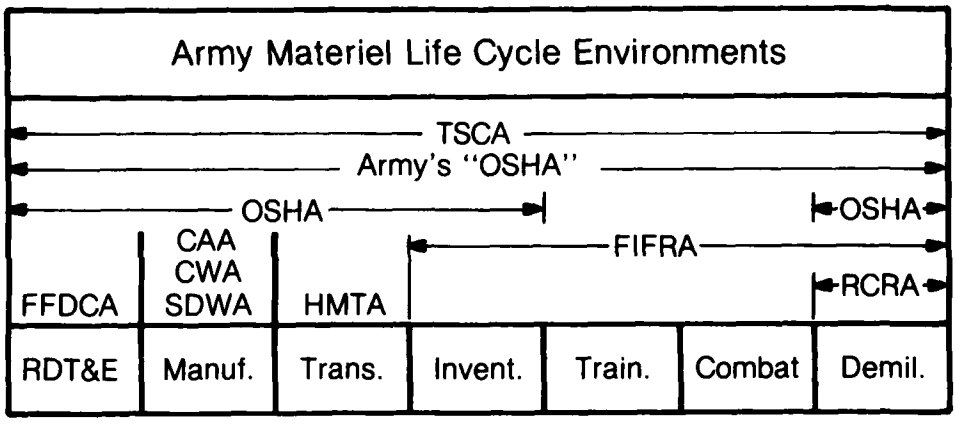


FIGURE 5 REGULATIONS IMPACT THROUGHOUT LIFE CYCLE

A materiel's life cycle is long, typically 35 years:

	Time
Concept	0
Prototype	8 yr
Testing	4 yr
Procurement	1 yr
Service Life	20 yr
Disposal/Demilitarization	2 yr
	35 Year Time Span

To avoid duplication of toxicology effort through loss of information, the DA should provide for central control and maintenance of the toxicology information base generated during the RTD&E phase which, when done correctly, handles all of the materiels toxicology requirements during its lifetime.

Requirements Summary

Identification of potential requirements is only the beginning of a requirements search methodology and, as noted above, various routes must be used to identify requirements.

A quantification of requirements was a program objective. This quantification can be viewed in many ways.

Simple View

A simple view of the toxicology requirement is shown in Table 12. It estimates requirements for major materiel categories, as a function of life cycle, into large, medium, small, uncertain or no toxicology needs. The categories having large toxicology requirements are the chemical and biological warfare activities, smokes and obscurants, munitions and explosives and pesticides, fungicides and rodenticides. The Other Support Equipment being a category for all miscellaneous unspecified materiel, also has significant requirements.

This simple view of requirements is more meaningful where each of the cited categories is only a summary of the subdivisions that make them up. Again, as illustrated in Figure 5, many levels must be reviewed before bases for the requirement code cited in Table 12 is found.

More Detailed View

A more detailed view of requirements resulted by reviewing the Army's chemicals and their uses, the types and numbers of weapons, and the number of manufacturing plants and locations within them and around them where hazards may exist. Appendix 8 presents background material on this approach.

Twenty-three different, general chemical uses were identified. Examples of chemical uses are explosives, fuel additives, dyes, etc.

For each general use for chemicals, there were many types. The fuel additive use for example, had seven types; antioxidants, biocides, corrosion inhibitors, fire control, icing inhibitors, lubricity improvers and static dissipators.

For each of the different types of a general use for chemicals there were estimated numbers of specific chemicals or mixtures to meet each of the types. The drug/vaccine use had seven types, one of which was antishock drugs. It was estimated that three drugs would be evaluated for the antishock application. As a result of applying this approach, a total of about 1,700 chemicals were projected to be in the RDT&E phase. About ten percent of the chemicals will be replacement for those items being phased out.

The analysis further identified approximately 200 weapons that potentially create a toxic hazard environment. There are, for example, eleven different surface-to-air missiles, twelve different personal defense, individual weapons, etc.

The analysis identified over 20 manufacturing plants, at least ten actively producing or loading munitions. Within each plant it was estimated there were at least two environments requiring toxicology evaluation. This is probably conservative when looking at the binary munitions plant as shown in Table 13. Three areas of toxicology exist: (1) associated with the chemicals involved, a process oriented area; (2) the occupational environment, which represents the exposures of personnel in the plant area and (3) the environmental health

TABLE 12 OVERVIEW OF REQUIREMENTS FOR APPLIED MAMMALIAN TOXICOLOGY RESEARCH/TESTING

Major Requirements Categories	Materiel Life Cycle[a]						
	RDT&E	Manufacturing	Transporting	Inventory	Training	Combat	Demilitarization
Aircraft	—	—	—	—	?	?	—
Missiles	S	?	—	—	M	S	?
Weapons (Not chemical, biological, small arms)	S	?	—	—	S	S	—
Tactical Combat Vehicles	M	?	—	—	S	S	—
Munitions, Explosives	M	M	S	—	M	S	S
Smokes & Obscurants	L	M	?	?	M	S	?
Drugs, Vaccines, Repellents	L	S(repellents)	—	—	—	—	—
Chemical & Biological Warfare[b]	L	L	M	M	L	M	S
Fuels, Lubricants, Additives	M	S	—	—	—	—	—
Clothing, Soaps, Dyes	M	M	—	—	—	—	—
Food, Water, Sanitation	?	M	—	S	S	?	—
Pesticides, Fungicides, Rodenticides	L	M	?	S	—	—	S
Medical Dental Devices	M	—	—	—	—	—	—
Other Support Equipment	L	M	S	S	S	S	S

(a) Need Code: L = Large, M = Medium, S = Small, ? = Uncertain (none or small)
(b) *Defensive biological warfare only and medical defensive chemical warfare only.*

TABLE 13 BINARY MUNITIONS PLANT

Chemicals Involved (Process-Oriented)

- Raw Material Chemicals
- Intermediate Chemicals
- Final Product
- Byproduct Chemicals
- Catalysts

Occupational Environment (Inside Plant to Site Boundaries)

- Specific Locations
- Criteria Preparation
- Monitoring for Conformance

Environmental Health (Area Surrounding Plant Site)

- Air
  - Chemicals
  - Interactions
    - Chemicals
    - Environmental Conditions
  - Degradation Products
- Water
  - Chemicals
  - Interactions
    - Chemicals
    - Environmental Conditions
  - Degradation Products
- Solid Waste
  - Chemicals
  - Interactions
    - Chemicals
    - Environmental Conditions
  - Degradation Products
- Routes of Exposure
- Standards Preparation

But the ties to:

1. How many chemicals?
2. What's known about each chemical toxicity?
3. What's the physical and chemical properties of each chemical?
4. What analytical techniques must be developed?

area, involving air, water and solid waste generated by the plant. Thus, the toxicology of a binary munitions plant can involve ten or more toxicology projects during the plant's design, startup and operational phases.

Cost Basis. Based on the material presented in Appendix 9, a cost of requirements was prepared. It included the cost associated with each of the four areas of toxicology: before testing, testing, parallel with testing and after testing. A range in cost for each of these toxicology task areas and the assumed typical cost are presented in Appendix 10. The estimated cost for all the tasks in each of the areas are:

Toxicology Task Area	Est. Cost for Task/Area
Before Testing	$0.39 million
Tier Testing	
0	$0.02 million
1	$0.04 million
2	$0.35 million
3	$0.85 million
Parallel With Testing	$0.18 million
After Testing	$0.04 million

Based on the assumed requirements list in Appendix 9 and the assumed number of new types per year (shown in Table 14 column three), the estimated volume for each of the four toxicology task areas was established. For example, there is estimated to be needs for 34 of the group of Before Testing Area Tasks, 19 for specific chemical, 10 with weapon environments and 5 with manufacturing plant environments. At a cost of $0.39 million/before testing group of tasks, the total identified cost for this area, is $13.3 million. When all the toxicology task costs are added, from the $13.3 million for before testing to the $0.3 million for after testing tasks, the total annual cost is $39.6 million. Of this amount, $23.3 million is due to testing, meaning testing is 60% of the total.

The ratio of tier 1, 2 and 3 testing costs is 1:1.9:4.9. The average industrial cost ratio might be 1:2:2, for a chemical industry, 1:1:1 or for a drug company, 1:7:3. The Army will tend to do more tier 3 testing because it is performance driven, i.e., it needs the product (typically a high performance capacity) but it also controls the use/user. Industry, on the other hand, is economics driven. It avoids chemicals that are questionable (i.e., if tier 1 tests indicate a potential problem). They do not generally control uses/users.

The identified portion of the requirements results from the summary presented in Appendix 9 of the information on the global Army toxicology requirements (Life Systems, Inc. 1981c). The latter, however, was felt to have identified no more than 50% of the total requirements. Also, the classified requirements and foreign materiel related requirements are estimated to represent an additional 3% and 2%, respectively. The total toxicology requirements volume is, therefore, close to $84 million (Table 15). If the unmet requirements are assumed to be 60% of the total, the volume of unmet requirements is $50 million. The testing portion (60%) of these unmet requirements would then be $30 million. If the chemical agent and drugs and vaccines type requirements are eliminated, the projected yearly unmet toxicology testing costs would be reduced to approximately $28 million or about 7% less.

TABLE 14 COST BASIS OF IDENTIFIED REQUIREMENTS

Toxicology Category	No. From Reqmts. List[a]	Est. New Per Year	Toxicology Tasks: Before Testing	Tier Testing 0	Tier Testing 1	Tier Testing 2	Tier Testing 3	Parallel with Testing	After Testing
1. No. of Chemical Uses	145	10		—— See Category (2) Below ——					
2. No. of Chemicals	1,691	170	19	8	35	20	10	10	5
3. No. of Weapon Environments	203	20	10	7	7	4	2	2	1
4. No. of Plants or Modifications	23	5		—— See Category (5) Below ——					
5. No. of Plant Environments	46	10	5	10	5	3	2	1	1
Total No. of Task Areas			34	25	47	27	14	13	7
Cost/Task, $(M) (Rounded Off)			0.39	0.02	0.04	0.35	0.85	0.18	0.04
Cost/Vol. of Tasks, $(M)			13.3	0.5	1.9	9.4	11.9	2.3	0.3

Identified Cost,	$39,600,000
Identified Cost Testing,	$23,300,000
Ratio Testing to Total Toxicology	0.6 to 1.0

(a) Without classified programs and limited requirements identification effort.

TABLE 15 PROJECTION OF YEARLY TOXICOLOGY & TESTING COSTS

1. Cost of Identified Toxicology Requirements	$40,000,000
2. Portion of Requirements Identified, %	50
3. Additional Classified Requirements, %	3
4. Additional Foreign Materiel Related Requirements, %	2
5. Cost Total Toxicology Requirements	$84,000,000
6. Percentage Requirements Unmet, %	60
7. Total Unmet Toxicology Requirements	$50,000,000
8. Ratio Testing to Total Toxicology	0.6 to 1
9. Total Unmet Toxicology Testing Requirements	$30,000,000

No quantitative or qualitative description of the Army's toxicology capability and capacity exists (except for AEHA). Therefore, no determination could be made of the exact unmet requirements. Sixty percent was assumed. No reason was found to expect the volume of toxicology requirements to change drastically over the next decade: The requirements existing now for items thru procurement will subside. But, in turn, the increased awareness of the toxicology related laws will cause more requirements offsetting the reduction normally anticipated as a bow wave is handled.

Cost Sensitivity. The accuracy of the cost estimates remains to be determined. This is the first known attempt to quantitatively estimate the unmet Army toxicology requirements. The number is almost certainly within one level of magnitude on either side (between $3 and $300 million).

If the number was 30% less or 50% more the approach to proceeding from this point on would basically be the same, i.e., the approach to meeting unmet requirements of $20 million per year or $45 million per year will be the same. The same activities will be needed:

1. Prepare justifications to obtain presently unbudgeted resources.
2. Develop a defensible justification for the added funding.
3. An analysis to determine how the unmet requirements can be minimized or eliminated.
4. An identification of the organization responsibility for the unmet requirements.
5. A cost/benefit analysis to determine the impact of doing or not doing the toxicology work.
6. Etc.

The medical requirements could be 30 to 60% of this. The analysis did not include the operational costs for such task activities as follow-up monitoring and medical follow-up estimated (Appendix 10) to be $150,000 per year, for each application that requires these efforts.

Global Requirements View

This approach is different than the simple or detailed views discussed above. It can be thorough by using many of the approaches cited in Table 8. An excellent beginning to the global Army toxicology requirements was made as part of the Study (Life Systems, Inc. 1981c). It, however, is still incomplete. The results, although representing a starting point for more accurate analysis, could not be completed within the time frame, funding scope, information provided or the skill level of the personnel. Nevertheless, the global Army toxicology requirements document contains 34 pages of requirements, candidates, structures and specific examples.

Alternative: How Much $10 Million Buys

An alternative approach suggested was to start with a fixed budget available for toxicology, such as $10 million. The amount of toxicology testing this could purchase, however, depends upon various ratios:

1. In-house work to extramural work.
2. Expenditures on testing versus funds for a facility.
3. The ratio of applied research to production testing.
4. Types of protocols used and the type of testing (number of Army-unique scenarios).

These and other questions made this technique ineffective in providing clear, concise definition of how best to spend $10 million on meeting toxicology requirements.

Ways to Review the Cost of Requirements

Another way to view the cost for the Army's toxicology requirements, when these requirements are not sufficiently defined to specify them, is to estimate the cost of not meeting them. This technique has merit since the itemizing of requirements is subjective, not clearly definable. Not definable because one toxicology test result in a sequence can stop the need for more toxicology work, while another test result can show more work is needed instead of proving no more work is needed. Figure 6 provides a summary of nine categories and a cost estimate for not meeting each of the requirements. A total of $80 million resulted. This was a one time estimate with no effort made to fine tune the result. Table 16 is the backup material generated to arrive at just one of the cost category estimates, delay in material fielding and retrofit.

Another way to view the requirements cost is to compare the DA with the top 20 or 30 American industrial firms doing in-house toxicology. The comparison should be in such categories as sales volume, size of work force, number of new products introduced per year, real estate holdings, number of manufacturing plants, number of states in which they operate, number of foreign countries in which they operate, etc. Then comparing the toxicology expenditures for these firms with and projecting costs for the Army, modified to reflect some of the differences in charters. This can lead to an estimate of a reasonable toxicology budget.

COMPARATIVE ANALYSIS

As shown above, although requirements exist, uncertainty also exists. This makes it difficult to specify the capability and capacity levels that should be added by the USAMRDC. It is essential that those that have to make the decision on how much money to spend for the added capability know specific requirements. The goal is to avoid inventing to just add more capabilities.

Just as the scope of the requirements vary between global DA and USAMRDC, so also does an evaluation of alternatives for meeting the unmet requirements. Table 17 reflects this variation, from an Armed Forces Institute of Toxicology to handle unmet global DOD needs to expansion of an existing facility (e.g., expand LAIR to meet USAMRDC toxicology testing requirements).

No.	Cost Category	Cost, $(Millions) 0.1 1.0 10 100	Total
1.	Delay Materiel Fielding & Retrofit	△	20
2.	Loss of Image[a]	△	4
3.	Medical Treatment of Exposed Personnel	△	2
4.	Medical Follow-up of Exposed Personnel	△	3
5.	Cost of Litigation	△	3
6.	Disability Compensation	△	15
7.	Survivor Benefits/Payments	△	15
8.	Installation Restoration	△	10
9.	Lost Time From Active Duty	△	8

Total $80

(a) Impacts personnel recruitment, & retention, Congressional support public support.

FIGURE 6 WAYS TO VIEW COST OF NOT MEETING TOXICOLOGY REQUIREMENTS

TABLE 16 BASIS FOR INDEPENDENT VIEW OF COSTS

System/Time Delay Levels (Penalty for Time Delay)	Reengineering Time Delay	Reengineering Engrg.[a]	Lost Image[b]	Lost Capability	Total
					Per 1,000 Items
1. Minor System ($10M)					
a. 6 mo (1%)	0.1	0.05	0.001	0[c]	0.15
b. 12 mo (3%)	0.3	0.15	0.003	0[c]	0.45
c. 24 mo (5%)	0.5	0.25	0.005	0[c]	0.76
d. Restart (80%)	8.0	4.00	0.080	0[c]	12.08
	8.8	4.45	0.089	0	13.34
					Per 30 Items
2. Major System ($100M)					
a. 6 mo (1%)	1.0	0.50	0.01	0.10	1.6
b. 12 mo (3%)	3.0	1.50	0.03	0.30	4.8
	4.0	2.00	0.04	0.40	6.4
Total Cost/Year	**12.8**	**6.4**	**0.13**	**0.40**	**19.7[d]**

(a) At ½ of time delay
(b) At 1/100 of reengineering time delay
(c) Waive requirement
(d) Assumes 1000 minor items and 30 major items; minor item cost is $10M, major item is $100M, and four lengths of minor delays, two of major item delays.

TABLE 17 TOXICOLOGY REQUIREMENTS LEVELS[a]

Level	Perspective	Concept
1.	Global DOD Needs	Armed Forces Institute of Toxicology
2.	Global Army Needs	Army Institute of Toxicology
3.	*The Surgeon General's Responsibility*	??
4.	USAMRDC's Perceived Responsibility	??
5.	USAMRDC with Added Full Service Toxicology Capability[b]	GOGO or GOCO at LAIR, Hunters Point, Etc.
6.	USAMRDC with Added Toxicology Testing Capability[b]	Expand LAIR Responsibilities

(a) Problem Definition Study focused on Global Army *Requirements* (no. 2) but adding only *testing capability* (no. 6).
(b) At one or more locations or add to each appropriate command laboratory

Testing Capability Exists

Toxicology testing sources exist (Table 18). They include existing laboratories, other armed service laboratories, the materiel manufacturers, etc. The capabilities of the available testing sources, however, do not meet all the Army's need. In many cases it is limited by one or more of the following: insufficient capacity, poor personnel quality or limited availability of qualified personnel, inadequate analytical chemistry capability, wrong type equipment, poor quality control, etc. Figure 7 schematically illustrates the available sources for toxicology. The Army's in-house capabilities are illustrated in Figure 8.

Options

This section discusses the options available to USAMRDC for meeting its unmet toxicology research/testing requirements or full service toxicology needs.

Five Basic Options

Five basic options have been identified including:

1. Government-Owned, Government-Operated (GOGO)
2. Government-Owned, Contractor-Operated (GOCO)
3. Contractor-Owned, Government-Operated (COGO)
4. Contractor-Owned, Contractor-Operated (COCO)
5. Combinations of the above.

The combination option includes some percentage of the requirements being done through each of the other four approaches.

Special Factors

Besides the five basic options, there are several other considerations that should be noted.

Five Versions Between GOGO and GOCO. It was cited that GOGO and GOCO represented two options. In reality, there are five variations in between as shown in Table 19. In each case the Facility would be Government-owned but that portion of the operation provided by a contractor varies - technician level only, professional level only, etc. This shows the concept of a GOCO can be at whatever level of control the USAMRDC wants. It also negates some of the USAMBRDL concerns.

Alternatives for COCO. The various COCO alternatives include:

1. Those available within continental United States (CONUS).
    a. For Profit.
    b. Not for Profit:
        1. Universities.
        2. Research Institutes.

TABLE 18 TESTING CAPABILITY EXISTS

Toxicology Testing Sources	Examples
• Existing Army Labs.	CSL, AEHA, USAMRDC's (e.g., BML)
• Other Armed Services Labs.	Air Force Aerospace Medical Research Lab.
• CONUS Contracting Labs.	Litton Bionetics, Hazelton Labs.
• OCONUS Contracting Labs.	Inveresk, Scotland
• GOCO Labs.	HHS / NIEHS / NSI; DOE / BNL / Assoc. Univ., Inc.
• Other Federal Agency Labs.	NCI, NIEHS, NCTR
• Materiel Manufacturers	DuPont, Dow Chemical

BUT THIS CAPABILITY

does not fit Army's need. Limited by one or more: Current Capacity, Personnel, Analytical Chemistry, Equipment, Location, Charter, Control, Quality, Etc.

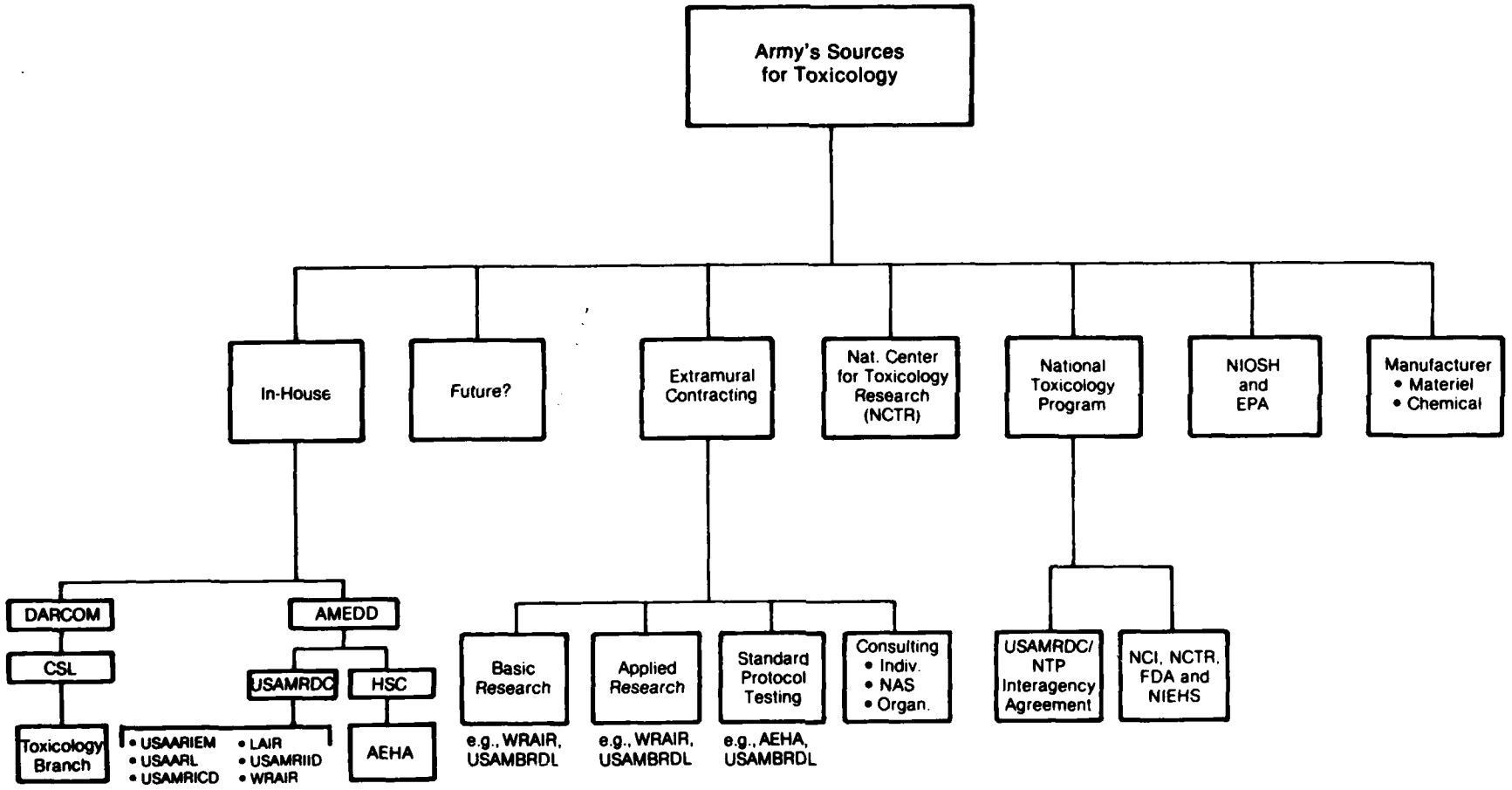


FIGURE 7 AVAILABLE SOURCES FOR TOXICOLOGY

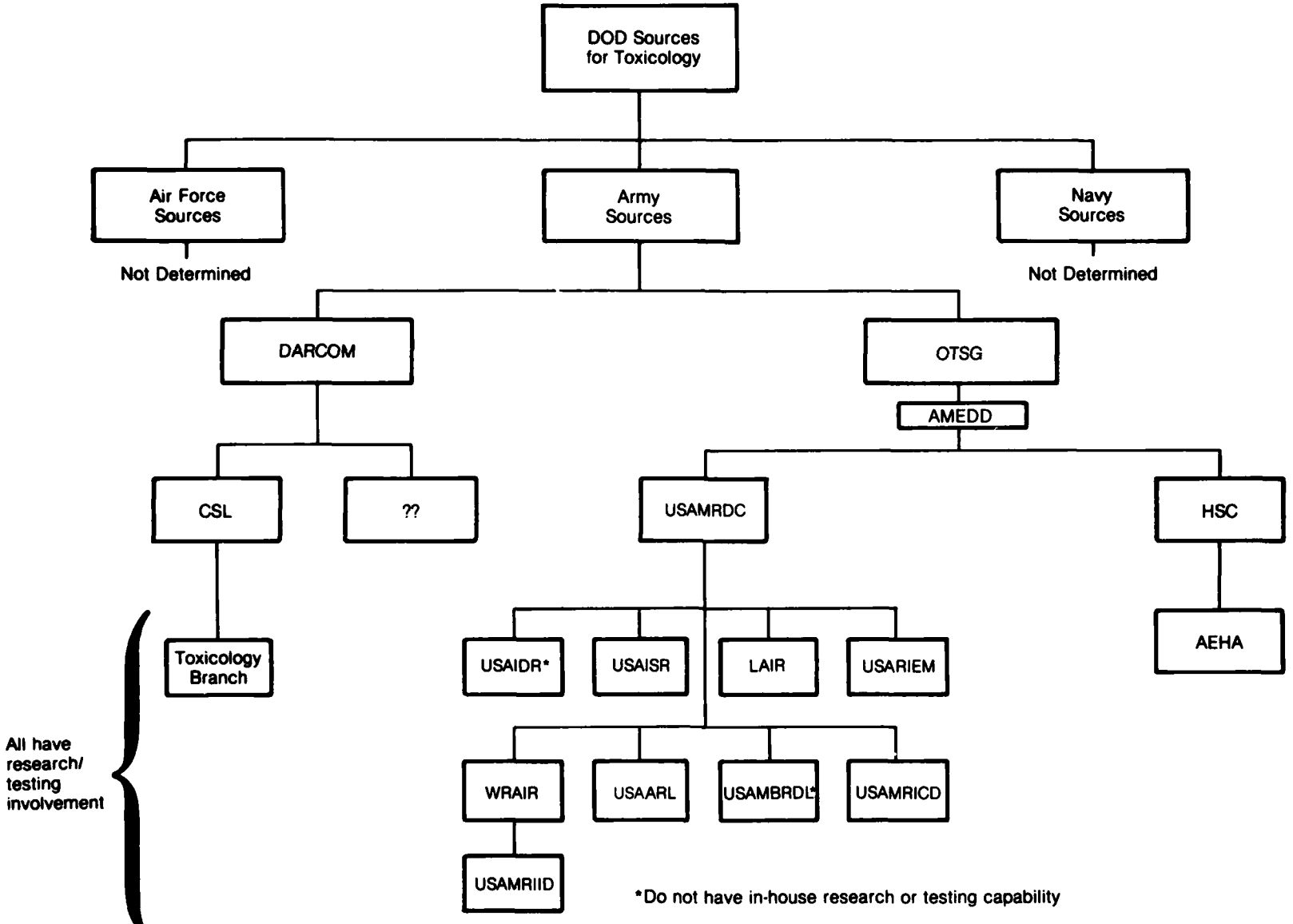


FIGURE 8 AVAILABLE LOCATIONS FOR TOXICOLOGY

TABLE 19 OPTIONS FOR TOXICOLOGY TESTING

Operator			
Business Only	Technical		Business and Technical
	Prof. Only	Tech. Only	
—	—	—	USAMRDC
USAMRDC	USAMRDC	Contractor	—
USAMRDC	Contractor	Contractor	—
Contractor	USAMRDC	USAMRDC	—
Contractor	USAMRDC	Contractor	—
Contractor	Contractor	USAMRDC	—
—	—	—	Contractor

2. Those available outside continental United States (OCONUS).

Of the mammalian toxicology services that are typically done on contract, three types stand out:

1. Basic research
2. Applied research
3. Production testing

Seldom will a university that specializes in basic research do applied research/testing and almost never production testing. Further, seldom will production testing organizations have the capability to do basic research.

Essentials of a COCO. Certain factors must all occur simultaneously before a known production testing organization actually becomes a source for doing the Army's toxicology work. These are:

1. It must agree to bid.

2. It must actually bid when the available need occurs.

3. It must be able to do the type of tests required (anything from an acute rodent oral to a combined oncogenic/general toxicology private inhalation).

4. Be balanced, i.e., have the specific toxicology capability and the supporting services needed. In the latter case analytical chemistry area is a particular problem when dealing with Army-unique chemicals.

5. Be cost competitive when found technically qualified by the procuring organization. A technically qualified contractor with a low price may win the procurement over a more qualified and preferred contractor asking a higher price. In a competitive procurement, a contractor that has a less than satisfying record of doing toxicology research/testing is hard to disqualify even if record is poor.

Contracting toxicology work is not without problems. It is difficult to find all the above items occurring simultaneously. This gives rise to the need for considering the other options.

It is unlikely a COCO can effectively handle three of the four major toxicology activities: Before testing, parallel with testing or after testing, as shown in Table 20. A GOCO may also be limited in doing the before and after testing activities. A GOGO can do all.

CONUS/OCONUS Needs

Both CONUS and OCONUS contractors that do toxicology testing are needed by the Army. The CONUS testing capability is needed to handle overloads and as a continuation of current approaches used (e.g., drugs and vaccines development, unique equipment development, etc.). The OCONUS testing capability is potentially needed to efficiently meet NATO requirements for doing work in participating countries and as a good way to conform to laws of a particular foreign country where the Army does business.

TABLE 20 TOXICOLOGY REQUIREMENTS

Toxicology Activities	Option		
	GOGO	GOCO	COCO
Before Testing	X	Maybe	No
Testing (Tier)			
1	X	X	X
2	X	X	X
3	X	X	X
Parallel with Testing	X	X	Doubtful
After Testing	X	Maybe	Doubtful

Unique Approaches Identified

Several unique approaches were identified for meeting the requirements. They included:

1. Contracting to a group of toxicology professionals in areas of limited supply to final design, oversee construction, and operate a dedicated Facility for the Army. It would require a firm Army commitment to have the work done at the Facility, but would help solve the staffing problem.

2. Having the National Center for Toxicology Research, Pine Bluff, AR, do Army tests. The Army may not even have to provide technicians or less skilled professionals as originally thought.

3. Leasing an industrial toxicology testing facility and contracting to an outside organization to manage it.

4. Purchasing an established industrial toxicology testing firm.

5. Utilizing (a) EPA's Center Hill Toxicology Facility in Cincinnati, Ohio which EPA is planning to close or (b) HHS's excess capacity at the new NIEHS Toxicology Facility, Research Triangle Park, North Carolina.

Evaluation Criteria

Major and minor criteria were identified for comparing alternatives.

Major Criteria

The major criteria include capability to handle the Army-unique scenarios, acceptance of results by regulatory agencies and the military, minimizing the number of government people required, flexibility to changing volume (especially decreases), the ability to build the Army's smart buyer ability and organizational memory, maintaining confidentiality of results and speed of response to a new requirement.

Minor Criteria

Minor criteria include ability to monitor QA, ability to provide full service, acceptance of the program by the public and politicians, availability of military security clearance, the time needed to start up the operation, the ability to hire supporting services, the ability to provide program continuity and various other issues.

Overall

Table 21 provides an overall relative comparison of performance alternatives. It results from a subjective, or in some cases, quantified, analyses to yield a summary comparison table between major performance alternatives. A detailed description citing the basis of each of the 180-plus inputs on the table exceeds the allowed report scope and guidelines.

TABLE 21 RELATIVE COMPARISON OF PERFORMANCE ALTERNATIVES

FACTORS	PERFORMANCE ALTERNATIVE			
	GOGO/USAMRDC	GOCO	COGO	COCO
MANAGEMENT EASE	Good	Best	Good	Poor
PERSONNEL				
No. of Gov't People Required	Large	Small	Large	Small
Ability to Staff	Unacceptable	Good	Unacceptable	N/A
Salary Structure	Unacceptable	Good	Same as GOC'J	Best
ANNUAL BUDGET AVAILABLE, $Millions				
1	Good	Can't afford facility	Better	Best
5	Good	Can't afford facility	Good	Best
10	Poor	Best	Poor	Better
20	Poor	Best	Poor	Good
40	Poor	Best	Poor	Poor
STARTUP TIME	Slow	Fast/Slow(?)	Slow	Fastest
QA MONITORING	Good	Best	Poor	Poor
ARMY UNIQUE	Good	Best	Poor	Poor
INDEPENDENCE	Poor	Good	Poor	Best
MAJOR CONCERNS	Inadequate Support	Loss of Control	No experience	Failure to perform
LIMITATIONS	1. Personnel Availability 2. Little Primate Capability 3. Capacity	1. Facility & Equipment Cost 2. Startup time	1. Any available?	1. Demand curtails available suppliers 2. Litle Primate Capability 3. No Army Unique Inhalation Capabilities
FULL SERVICE				
Capacity	Possible	Possible	Not as possible	Not as possible
Capability	Not as possible	Possible	Not as possible	Possible
Before Testing	Yes	Yes	Yes	No
Parallel With Testing	Best	Better	Good	Poor
After Testing	Best	Better	Good	Poor
Acute	Small	None	None	Large
Subchronic	Small	None	None	Large
Chronic	None	None	None	Medium
HIRE SUPPORTING SERVICES				
People, Professional	Not as possible	Possible	Possible	N/A
People, Technicians	Not as possible	Possible	Possible	N/A
Level of Effort	Not as possible	Possible	Possible	N/A
Capability	Not as possible	Possible	Possible	Possible
FLEXIBILITY TO CHANGING VOLUME				
Increases	Poor	Better	Poor	Best
Decreases	Poor	Good	Poor	Best
SPEED OF RESPONSE	Fast	Fastest	Faster	Slow
BUILDS ARMY'S				
Smart Buyer Ability	Best	Good	Better	Poor
Organizational Memory	Best	Good	Better	Poor
PROGRAM CONTINUITY	Best	Good	Good	Poor
ACCEPTANCE				
Regulatory Agency	Good	Better	Better	Best
Military	Best	Good	Good	Poor
Public	Good	Good	Good	Good
Political	Poor	Good	Poor	Best
PRIVACY OF RESULTS	Best	Good	Good	Poor
SECURITY	Better	Good	Better	Good
OTHER ISSUES				
Ability to use LAIR	Yes	Yes	No	No
Ability to use Hunters Point	Yes	Yes	No	No
NATO Acceptable	Possible	Not as possible	Not as possible	Best (if OCONUS)
Applicable to DOD	Not as possible	Possible	Not as possible	Not possible
Analytical Chemistry	Good (once dvlpd.)	Good (once dvlpd.)	Good (once dvlpd.)	Unaccept to good
Load Leveling (Facility)	Good	Better	Good	Poor
Peak Loads (People)	Good	Better	Good	Poor
Innovation	Best	Good	Good	Good

(a) The following comparisons were used for:
Quality or Preference — unacceptable, poor, good, better, best
Probability — possible, not as possible, not possible
Numerical — none, small, medium, large
Time — slow, fast, faster, fastest
Go-No-Go — yes or no

The GOGO, GOCO and COGO are not currently available to provide added testing capability. Since it is based on familiarity with an analysis of the four alternatives, no absolute judgment can be made. The relative comparison illustrates the distinction among the alternatives.

From a cost viewpoint and for the short term, COCO is best, then COCO, GOCO and finally, the poorest GOGO. In the long term, GOGO was considered best, then GOCO, COGO and finally, the least attractive COCO. The latter results from the failure to provide an Army's smart buyer and organizational memory capability.

Cost Comparison. A comparison was made between a COCO approach and a GOGO or GOCO approach based upon four specified general toxicology studies. The results are summarized in Table 22 utilizing cost data for each of the four studies presented in Appendix 11. In all cases the GOGO and GOCO are 22% lower in price. This is because of the assumptions used for the overhead, G&A and fee for each of the three options as indicated at the bottom of Table 22.

A mini-sensitivity analysis was also completed. It compared the total cost assuming different numbers of the four general toxicology studies, i.e., four of one, three of another, two of a third and one of the fourth. Although the total dollar value varies depending upon which study was being carried out the most frequently, the cost comparison remained in the same ratio because of the rates assumed.

General Comparison Results

All sources must be used to save the Army the most money. This includes active solicitation of other federal agencies, such as those in the NTP, to carry out some Army toxicology work. In addition, manufacturers and materiel development contractors should be required to do the work where appropriate.

OTHER SUBJECTS STUDIED

During this Study various subjects were studied as special projects. The results of some of these are summarized below.

Construction Approvals

Four documents were identified that relate to constructing or modifying government facilities and the allowability of the new start or expansion of a Government-Owned Contractor-Operated (GOCO) facility.

The issue of whether military construction Army (MCA) funds are needed is addressed in Army Regulations AR 415-15, -25 and -35. The issue of adding new capability to or starting a new GOCO are reviewed in Army Regulations 235-1 "Industrial Activities and Labor Relations, Commercial/Industrial-Type Activities (CITA)," and OMB Circular No. A-76 (Executive Office of the President, Office of Management and Budgets 1979), respectively. Evaluations of these documents indicate MCA funds may be required and a formal cost analysis as defined in AR 235-1 or OMB Circular No. A76 most likely will be required. More detailed evaluation will clarify the situation.

TABLE 22 COMPARATIVE COCO COSTS $(000)

No.	General Toxicology Study[a]			Sensitivity Analysis							
		No.	Cost	No.	Cost	No.	Cost	No.	Cost	No.	Cost
1	Chronic Rodent Inhalation	1	613	4	2,452	3	1,839	2	1,226	1	613
2	Subchronic Rodent Oral	1	56	3	168	2	112	1	56	4	224
3	Acute Primate Inhalation	1	39	2	78	1	39	4	156	3	117
4	Subchronic Primate Inhalation	1	196	1	196	4	784	3	588	2	392
	Total COCO[b]	4	904	10	2,894	10	2,774	10	2,026	10	1,346
	Total GOGO/GOCO[b]	4	701		2,246	10	2,153	10	1,573	10	1,044

(a) One species.
(b) Cost Basis (GOGO and GOCO are 22% lower in price). (See also Appendix 11.)

	COCO	GOGO	GOCO
Overhead, % of Total Direct Labor	115	90	120
G&A, % of Factory Cost	10	5	0
Fee, % of Total Cost	20	0	9

Load Leveling

A project was completed to evaluate load leveling as a technique to prevent overloads of a toxicology testing facility. Load leveling will be required but methods were found to minimize periodic peak demands on the Facility and its equipment. These included effective management, use of outside sources, deletion of the requirement and acquisition of standby capability.

Handling Peak Demands for Personnel

An evaluation was made to determine if this would be a problem, if it could be avoided and how to minimize it. The results are summarized below.

Peak demands for certain personnel (e.g., veterinarian pathologist at the end of a chronic experiment) will occur. Although controllable to an extent, it will not be unavoidable because of the nature of toxicology testing. Protocols define what and when work has to be done. Four techniques were reported on to minimize overload of personnel including:

a. Effective management.
b. Utilization of outside supporting services.
c. Expand the equipment's capability to minimize the need for limiting personnel's time.
d. Use of lower level personnel to reduce burden on personnel.

Potential GOCO Operators

A project identified potential GOCO facility operators. Sixteen organizations were found: Four were universities, four were nonprofit organizations and eight were industrial firms.

What Testing Should be Started Now?

This project determined:

a. What testing can be started immediately?
b. When drug and vaccine type testing can be initiated?
c. When testing to support Navy and Air Force requirements can be initiated?
d. When a GOCO can be ready for full capability testing?

Start Immediately

The only testing that could be initiated immediately would be those tests that would be carried out by COCO. Completion of a new or renovated facility would take two to seven years depending upon scope and approval cycles. The ability to identify a contractor facility available for leasing by the Army would require a minimum of one year.

In a newly started GOCO, such as the LAIR, the dermal and ocular work could begin readily within 12 months and oral toxicology using rodents could start within 12 to 18 months.

Drug and Vaccine Type Testing

The program concluded the toxicology being completed as a part of drug and vaccine developments should remain within their current laboratories. Any transfer of these toxicology functions to a new facility would contribute little and result in significant lack of coordination in the Army's development programs.

Supporting Navy and Air Force Requirements

Testing for the Air Force and Navy could not be initiated for at least six years. This is based upon the Army's requiring three years to reach operational status, two years for demonstration and meet Army's startup needs and one year to effect transfer of funding from the Navy or Air Force to the Army. If the latter was carried out in parallel, the time could be cut to five years. The Facility cannot, however, be justified assuming work would be done for the Air Force or Navy (Life Systems, Inc. 1981a).

Time Needed to be Ready for Testing

As shown in Table 23 the time required to renovate a Facility would range from 49 to 78 months provided an OMB cost comparison was needed. Ten additional months would be needed if the Facility was a new one. Without the OMB process, the time could be decreased to approximately three to five years. Figure 9 illustrates these time frames. The smaller the size of the Facility the quicker it can be implemented.

Remote Toxicology Site for Hazardous Testing

A project was completed to study the option of a remote site for carrying out the more risky types of mammalian toxicology testing. This site would test chemicals that are particularly hazardous but also important for the Army's unique mission(s) or weapon(s).

Although the remote concept is attractive, it is not cost effective and would be difficult to staff. An existing capability such as the Chemical Systems Laboratory which works with highly toxic materials, would be a more cost-effective location for handling these special medical requirements.

Effects of Maintenance Cost

A project was completed to establish the impact of facility and equipment maintenance costs on option selection. Equipment maintenance costs were projected at 10% of the initial equipment's cost for each year of use. The facility maintenance cost for the first two years of operation was 1% of the total facility cost and 0.1% for the years three through ten.

The project concluded maintenance costs would have little influence on the option selected.

Selling Testing to Other DOD Organizations

A project determined the merits of the Army using its Facility to perform testing for the Air Force and Navy. It identified advantages, such as lowering

TABLE 23 TIME NEEDED TO BE READY FOR TESTING

Program to Date	5/79 to 4/81 Time to Accomplish, Months		
Milestone/Activity	Fast	Likely	Delta If New Construction
Facility Specification	6	9	—
OMB Cost Comparison	14	21	—
Architectural/Engrg. Prep.	8	13	—
Bid	1	2	—
Construction	20	33	10
Total, Mo	49	78	10
Total, Yr	4.1	6.5	4.9 to 7.3
Without OMB Process, Yr	2.9	4.8	4.4 to 5.6

(a) Debugged and fully operational

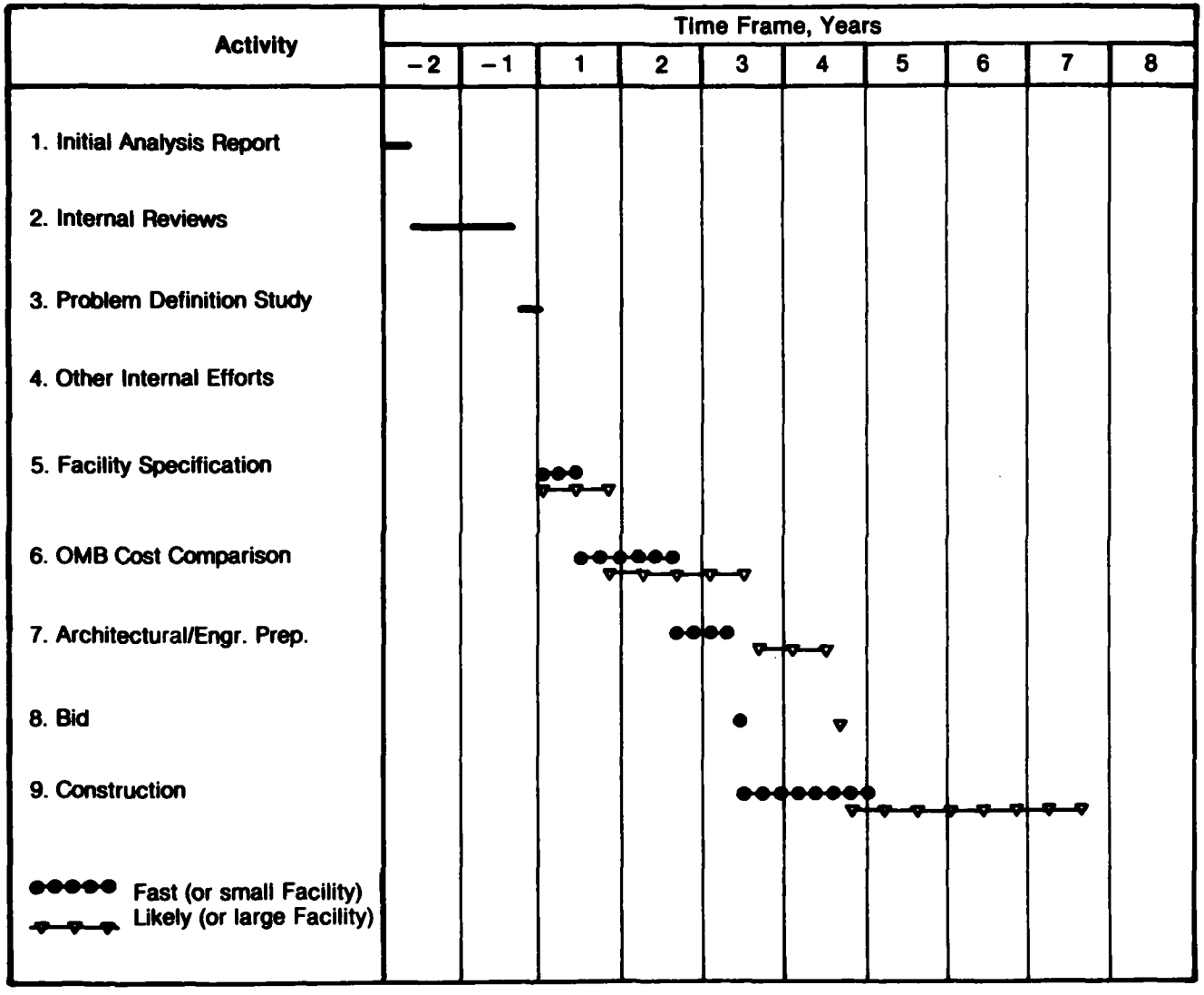


FIGURE 9 CAPABILITY DEVELOPMENT SCHEDULE

the military's total cost by avoiding duplication of effort when utilizing a common organization. The disadvantages were also identified, such as the added cost to the Army to initially incorporate this greater-than-needed capacity which would not "pay-for-itself" until other DOD departments finally used it.

A review of OMB Circular No. A-76 indicates, "It is not intended that agencies create or expand capability for the purpose of providing commercially-available products or services to other agencies". The question remains to be resolved, however, whether DA is viewed as an agency or DOD is viewed as an agency.

WHAT WAS DONE BUT NOT INCLUDED IN THIS REPORT

Many other activities were completed under the requirements and comparison efforts of the Study. These efforts were reported directly to Army program personnel. Included among these studies were:

1. Identification of foreign toxicology testing laboratories.
2. A definition of DARCOM Commands, their missions, those with Project/ Program Managers and work force, military and/or civilian.
3. Identification of which other agencies are making or have made decisions to have GOCO toxicology facilities.
4. Identification of other government toxicology testing laboratories that could be used by the Army (e.g., including results of other studies (Development Planning and Research Associates, Inc. and ICF, Inc. 1981)).
5. Advantages or disadvantages of a central manager or focal point for all or a portion of the Army's toxicology requirements.
6. Results of visits to candidate contractors and agencies.
7. The impact of priority setting on requirements.
8. An analysis of shortages in toxicology: personnel types, animals and testing capability.
9. Analysis of desired rate of startup toxicology testing.
10. Process for gathering information on potential toxic substances.
11. Generation of a data base on toxicology testing costs.

CONCLUSIONS

The following are some of the conclusions resulting from the requirements identification and comparison of alternatives portion of the Study:

1. Army toxicology requirements exist beyond those being met. A systematic method to identify them does not exist nor does the charter seem

to belong to a particular organization. The Study identified 13 different ways to approach toxicology requirements identification. Five of the approaches were used on the Study. The Army is in many different industries which require different approaches to toxicology requirements. This results, in part, because different regulations apply to different industries.

2. The Study had as its goal the identification of global Army requirements. This is counter to the preparation of a specific list (e.g., 35 toxicology testing requirements) that certain individuals within the MRDC desired. The Study identified that a major part of toxicology requirements is associated with tasks focused on eliminating the need for toxicology testing, to provide assistance to the materiel developer (DARCOM), etc. These do not appear on a testing requirements list.

   A requirements identification framework was identified using a top down approach tied to the five procurement categories used by the Army. The requirements framework contained over 30 pages of areas where toxicology is needed or most likely will be needed. These must now be screened for the hazards that would require toxicology activities on a case by case basis. As an average, it can be projected each would require 8 to 15 hours to evaluate. No quantitative or qualitative description of the Army's toxicology capability and capacity exists so the unmet requirements cannot be defined without more time to establish specifics.

3. The Army will require mammalian toxicology services "forever". It is not a one-time thing, done once and for all. The Study concluded there are more requirements than were identified because the systematic approach defined by the Study could not be used fully within the program's scope. Further, the growth and requirements will multiply as the many people working on materiel development and many users during its life cycle start to identify the hazards associated with using chemicals and the legal responsibility they have to report any suspected situation that involves toxic substances increases.

4. Managers of existing, ongoing toxicology programs, i.e., chemical warfare, drug and vaccine developments, etc., are not inherently sources of unmet requirements. They do not have the charter, budget or staff to search out unmet requirements except in their materiel area.

5. Some toxicology requirements should not be grouped with the others. The toxicology, for example, that is associated with health hazard assessments should be grouped with other issues within that program. These toxicology requirements include those that relate to weapons which generate hazardous environments including toxic environments. Other toxicology requirements that should remain separate from the others include the normal drug and vaccine development processes, offensive and defensive chemical warfare, defensive biological warfare, etc.

6. Many unmet toxicology requirements should be grouped together such as those associated with specific laws including the Toxic Substance Control Act, the Resources Conservation and Recovery Act, etc.

7. The methodology that was used to evaluate the Army's toxicology requirements can serve as a model for addressing the more complex occupational health and health hazard assessment requirements for the global Army.

8. Access to toxicology data bases and interpretation of the data are needed for chemicals that are serious candidates for new Army materiel before final selection of those chemicals or mixtures.

9. Once a toxicology requirement is suspected, a broad range of questions must be answered varying from is there any information in the literature to support the suspicion the chemical or environment might be toxic to humans to who is responsible for the situation having the suspected toxicology requirement, what is the priority of this program relative to others and the time frame of this priority and what does the cost/benefit analysis indicate regarding merit of actually initiating testing.

10. The boundaries between the medical and nonmedical organizations within the Army are unclear as are those between the HSC and USAMRDC. Documentation reflecting the role of USAMBRDL in toxicology did not reflect a clear statement of toxicology responsibilties. This complicates toxicology requirements identification.

    No document was found or provided that clearly addresses the rules The Surgeon General uses for employing toxicology data to the development of human exposure criteria as they are needed for weapons use, materiel manufacturing, environmental health issues concerning personnel in and around Army controlled activites, etc.

11. Various approaches for assigning toxicology responsibility exists:

    a. Assign it to the equipment developer (e.g., DARCOM) and have toxicology evaluations be a routine part of the equipment development process. The Surgeon General would develop only criteria and standards.

    b. The toxicology responsibility would be part of the equipment evaluation process, i.e., part of the test and evaluation organizations mission. In this case, AMEDD would arbitrate technical matters and assist DA in making trade-off decisions with no conflict of interest or enforcement authority.

    c. Responsibility resides in AMEDD which assumes proper staffing, personnel qualifications, funding available and follow-up assessments. Further, it assumes that within DARCOM the information can be translated into design criteria.

12. The cost to meet unmet toxicology testing requirements will be between $30 million and $50 million per year for the global Army. If 30 to 60% of the requirements are the responsibility of the medical organizations, the annual budget would be about $10 to 20 million for just the lower estimate. These levels are far more than the maximum amount of money that could be pared from other USAMRDC programs.

13. The USAMRDC is understaffed for performing the unmet toxicology requirements. An organization the size of the Army and in as many industries as the Army is in, has such an extensive number of toxicology related efforts that the USAMRDC, as a focal point, cannot handle the Army's needs with one laboratory, such as USAMBRDL. The latter is understaffed to do the job and has a focus more directed toward basic than applied, production type testing or the requirements identification and analysis process.

14. The requirements and funding identification system should be identified before a new capability at a defined capacity is operational.

15. The DARCOM materiel life cycle management process provides only limited entry to the toxicology aspects of materiel. This occurs through the Health Hazard Network Block Nos. 158 and 318. The life cycle network process, however, is a systematic method that can be adapted to supporting DARCOM in the area of toxicology.

16. A decision is not needed to proceed with building a toxicology testing Facility but one to implement a program to meet USAMRDC's responsibilities for its unmet medical toxicology requirements. These responsibilities include a lot more than toxicology testing. It starts with a defensible plan that shows what USAMRDC has been chartered to do, what its current funds can do and what it will not be able to do because the money or the staff is not being provided to do it. A plan is needed to justify a program that will be required for as long as the Army and society places a premium on human health. A majority of unmet requirements are resulting from the increased awareness of the hazards to human health because of the environments people are exposed to.

17. The significant (30 to 60%) unmet requirements are not physician/medicine oriented although they do relate to human health. A decision is needed, therefore, whether the medical thrust of USAMRDC is compatible with meeting the unmet Army requirements for toxicology, e.g., the analysis work done before testing, the communication work done in parallel with testing and the after testing portions. Further, the requirements of such laws as TSCA do not warrant the skill level of medical personnel such as physicians.

18. The Army's unmet toxicology requirements cannot be met with existing Army facilities. There are existing civilian contractual services that could be used, but with penalties; higher costs being paid, acceptance of lower quality on certain toxicology programs, no smart buyer capability involved, loss of Army memory and no development of Army-unique capabilities.

19. Although excess Army facilities and equipment are not available to do the additional toxicology activities, new capabilities and capacities can be added to existing Government facilities, e.g., USAMRDC's LAIR.

20. Although the Army has inhalation facilities of its own, no Army-unique inhalation exposure capabilities exist. The latter would represent an upgrade of existing or added facilities to meet Army-unique scenarios such as short-term, repeated exposures, of intense concentration under unique environmental conditions and associated stress conditions. This capability includes equipment for generating the hazards (chemicals and their physical forms) and inhalation chambers that simulate the environment where the toxic hazard exists or will exist. This capability should not be incorporated into a contractor's or other Government agency facility but into an Army controlled facility. Studies of special interest include:

    a. Combined stresses (vibration, heat, pressure, plus chemical exposure).
    b. Exposure to mixtures of chemicals.
    c. Exposure patterns: high concentration - short duration.

    Facilities are not currently available to meet these requirements. It is unlikely that they will be developed without direct funding and research by the Army.

21. The new facility should do more, for example, than toxicology testing. There are several reasons for this: testing is only a part (albeit an expensive one) of the Army's toxicology needs. Limiting the facility to testing leaves the rest to be resolved "later". Other reasons include more effective use of personnel, providing a means to recruit and retain quality personnel, incorporating basic research and training needed to reduce future Army costs, etc.

22. A single performance mechanism or source (GOGO, GOCO, COGO or COCO) is not capable of providing the needed full service capability. Multiple sources, both in-house and extramural, are required. The selection of which combination of alternatives should be used depends upon:

    a. Which Command is responsible?
    b. What portion of the resources will be available from the Facility itself?
    c. Complex set of interrelating factors.

23. A firm recommendation was not made to establish a GOCO at the new facility because data needed to provide answers to the following questions were not available:

    a. What will be the total money available as a function of time?
    b. What is the time frame for startup?

c. What rate of buildup should be planned?
d. What number of people will be available before, during and after construction?
e. What equipment and what services will be provided by the host Government organization?

24. The development of a separate, remote location by USAMRDC to do portions of very toxic or very hazardous toxicology testing is not cost effective.

25. Although new technology is needed to obtain information on concomitant effects of chemicals and environmental conditions (e.g., temperature, vibration, stress), this is not as high a priority as identifying Army areas of vulnerability because of toxic environments and supporting the materiel developer. A behavioral toxicology program will be needed in the future but it is not a requirement that needs attention at the expense of current unmet requirements.

RECOMMENDATIONS

The following recommendations were made as a result of the Study:

1. A central focal point should be established for assembling and communicating toxicology information. This Army toxicology information focal point would eventually become the basis of a toxicology information system. This system would provide:

    a. A risk/benefit analysis capability.
    b. Continuous evaluation of RDT&E for toxicology requirements (at least one time per year).
    c. A focus on how to avoid the testing in the first place.
    d. Data on all known sources of toxicology solutions; in-house, extramural, manufacturer, etc.
    e. The knowledge of who's doing what toxicology, why, when and where?
    f. The Army's memory and data base on what was done, recognizing the typical life cycle is 35 years long.

    There should not be central management/control of the Army's toxicology since many of the toxicology activities should not be centralized, i.e., that associated with:

    a. Drugs and vaccines development.
    b. Offensive and defensive chemical warfare.
    c. Defensive biological warfare.
    d. Health Hazard Assessment Program.
    e. The charter of the Army's AEHA.

2. A project should be carried out to determine the availability of three toxicology testing laboratories already within the government.

    a. HHS's NCTR Toxicology Facility, Pine Bluff, AR.
    b. EPA's Center Hill Toxicology Facility, Cincinnati, OH.
    c. HAS's NIEHS Toxicology Facility, Research Triangle Park, NC.

3. A project should be initiated to evaluate the possibility of a single service facility, with tri-service integrated, as opposed to coordinated management, for providing unmet toxicology requirements. This organization should utilize the scattered facilities within the DOD. Primary leadership should be determined by whomever has the greatest need, best capability and most experience of the three services.

4. Establish a formalized process for identifying unmet toxicology requirements, their basis (regulatory, nonregulatory) and command responsible for meeting, hence paying for, meeting the requirements.

   The effort should involve assignment of responsibility for determining what materiel is under development in each of the four major RDT&E funding categories, especially those in 6.3 and 6.4. The latter represent programs having the highest priority for screening for toxicology requirements. The effort should also include identifying what is USAMRDC's responsibility for the Army's conformance to the Toxic Substances Control Act. This law specifically requires that EPA be notified of any identified substantial risk, with litigation penalties if this does not take place (Section 8(e)).

5. A project should be carried out whereby representatives of DARCOM/CSL and OTSG/USAMRDC meet to establish a cost-effective, ongoing method to define unmet toxicology requirements and establish the responsibilities of each. The program would lead to an upgrading of the requirements list prepared on the Study. The activity should also better define the boundaries between medical and nonmedical, USAMRDC and HSC and those of various laboratories within USAMRDC, especially USAMBRDL.

6. A project should be carried out to quantify the existing USAMRDC toxicology capability and capacity, utilizing information questionnaires prepared under the program.

7. A determination must be made regarding the need for MCA funding and the cost analyses that must be prepared before new capability and capacity can be added (e.g., OMB Circular A-76, AR 235-1).

8. Proceed with the addition of added capability and capacity only after balancing which specific requirements will be met with the facility, who is responsible for these requirements and, obtain commitment of the money to pay for the testing, finalize the alternative sites (LAIR, NCTR, etc.) and characterize in more detail the Army-unique capability needed.

9. Implement the technology transfer whereby techniques generated as a result of this Study can aid in the Health Hazard Assessment Program development and simultaneously remove the toxicology done as a subset of health hazard assessment from the overall requirement into the HHA program.

10. A decision should not be made to go ahead with building a toxicology testing facility. The need is to implement a program to meet USAMRDC's responsibility for its unmet medical toxicology requirements. These responsibilities, however, include more than toxicology testing. It starts with a defensible plan that shows what USAMRDC has been chartered to do, what its current funds can do and what it will not be able to do because the money is not being provided to do it. It then becomes the decision by those providing personnel and money (OTSG and DCSRDA).

11. The unmet toxicology requirements should not use funds needed by other USAMRDC priority programs (e.g., overpressure standards setting, chemical agent prophylaxis). But to avoid toxicology's crisis "tomorrow," USAMRDC must plan in detail, justify and have the DA set the money aside to meet the DA's unmet, priority toxicology requirements.

12. A GOCO should not be established at LAIR, Hunter's Point or elsewhere if the budget available is $5 million or less per year, if the funding from users is not committed to, or if there are not enough USAMRDC people available to staff its selected portion of the Facility's operation. If the annual budget is $10 million or more per year, and the requirements identification system is implemented to obtain the money from the organizations responsible for the requirements, a GOCO facility could be implemented.

13. The LAIR was considered a more optimum facility than Hunter's Point because of the condition of the facility, the added services it can provide, saving the USAMRDC money, and because of its location, which enhances the hiring of personnel.

14. No basic toxicology research should be started (new) until the unmet requirements are fully identified, plans laid out to meet these requirements, and effective support of Army materiel developers demonstrated. The existing basic toxicology research program implemented through USAMBRDL is out of proportion when viewed from the failure to successfully identify and plan USAMRDC's unmet toxicology requirements.

15. Business should continue as usual for those efforts which have long been using toxicology and have funds provided as part of their existing funding cycles (e.g., drug developments, chemical warfare).

16. Implement the project to define a questionnaire that will rapidly screen the toxicology requirements of major Army programs. The purpose is to enable program managers to answer questions which would provide an indication of whether toxic hazards exist within his program and if so the areas where they may exist.

17. The environmental toxicology efforts should be grouped with the health efforts, recognizing not all health efforts simultaneously have environmental toxicology efforts.

18. A position paper should be prepared which clarifies why existing Federal agencies doing toxicology work do not solve the Army's toxicology needs. It would reflect, for example, that these agencies reject most of the Army's requests because (a) there is not sufficient volume to warrant the attention of the agency/NTP, (b) there are not sufficiently large numbers of civilian population involved to warrant the material obtaining a high priority rating and (c) the basic research the NTP does, while applicable to toxicology technology users, does not provide the fundamental information needed for Army-unique exposures.

    A list should be prepared citing the requests the Army has made to NTP asking for support. This should be included with the justification for the USAMRDC's budget request for funding.

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APPENDIX 1

ACRONYMS AND TERM DEFINITIONS

AAALAC - American Association for Accreditation of Laboratory Animal Care.

Acute Effects Tests - Tests employed to determine the immediate or short-term effects following a single chemical exposure.

AEHA - Army Environmental Hygiene Agency

AMEDD - Army Medical Department.

AMTR - Applied Mammalian Toxicology Research/Testing.

Applied Mammalian Environmental Toxicology Research - Studies performed to predict adverse human health effects associated with environmental exposures to air, water and soil pollutants. These exposures affect the general population via contaminants in ambient air, drinking, bathing and swimming area water and the food chain (eating of meat, fish, seafood and vegetables). These exposures are not associated with the individual's occupational exposure.

Applied Mammalian Toxicology Research - Studies aimed at measuring the effects of chemicals in mammalian systems using established test protocols. Excluded are all human epidemiological studies, non-mammalian testing, such as mutagenic studies tests to determine the adverse effects of ionizing and non-ionizing radiation and physical factors such as pressure, temperature, noise and vibration. Applied toxicology research provides for data base and criteria and standards development.

AR - Army Regulation.

Archives - The area used to store all raw data, notes, specimens, slides and other information generated as the result of a toxicology study.

Basic Toxicology Research - Studies aimed at understanding the effects and fate of chemical in biological systems including modifying factors. It includes the studies to develop methods for reducing the future cost of toxicology testing and improving extrapolation of test data, including concomitant effects.

Behavioral Dysfunctions - Disturbances in behavior.

BML - Biomedical Laboratory. This facility has been redesignated USAMRICD, United States Army Medical Research Institute of Chemical Defense.

Built-in Equipment - Fixed, nonmovable equipment that is either connected to the floor, walls, or ceiling and/or is connected to a piped water line, fixed power line, fixed wastewater line, or intake or exhaust vents.

Carcinogenicity - The induction of cancer

CARDS - Catalog of Approved Requirements Documents.

CCA - Clean Air Act (1970).

Chronic Effects Tests - Tests employed to determine the long-term effects of multiple chemical exposures.

CITA - Commercial/Industrial-Type Activities.

COCO (Contractor-Owned, Contractor-Operated) - A function performed by contractor personnel in a contractor-owned facility. Material and equipment may be furnished by the Government or by the contractor.

COGO (Contractor-Owned, Government-Operated) - A function performed by Government personnel in a contractor-owned facility. Material and equipment may be furnished by the Government or acquired for the Government by the contractor.

Control Article - Any chemical, substance or mixture of materials that is administered to the test system in the course of a study for the purpose of establishing a basis for comparison (often used synonymously with Referenced Standard).

Cost Comparison - An accurate determination of whether it is more economical to acquire the needed products or services from the private sector or from an existing or proposed Government commercial or industrial activity.

CPSA - Consumer Products Safety Act (1972). A statute defining some of the responsibilities of the Consumer Product Safety Commission (CPSC).

CPSC - Consumer Products Safety Commission.

Criteria - Levels and/or a set of conditions established to serve as guidelines for evaluating the general acceptability and risk of a situation. Criteria are not enforceable in a court of law.

CSL - Chemical Systems Laboratory. Part of US Army Armament Research and Development Command

CV - Curriculum Vitae.

CWA - Clean Water Act. Title assigned to the 1977 amendments of the Federal Water Control Act.

DA - Department of the Army.

DARCOM - Materiel Development & Readiness Command.

DCSRDA - Deputy Chief of Staff for Research, Development and Acquisition.

Debug - Efforts to correct initial defects or malfunctions in equipment process or procedure.

DHEW - Department of Health, Education and Welfare; now the Department of Health and Human Services and the Department of Eduction.

DOD - Department of Defense.

DOL - Department of Labor.

DOT - Department of Transportation.

EPA - Environmental Protection Agency.

Epidemiology - That field of science which deals with the relationships of various factors as determinants in the distribution and frequency of disease or death in the human population. As such it attempts to identify by actual human experience the nexus between chemicals and their effects on people.

Equipment Acquisition - All ordering and receiving activities for selected items.

Equipment Categories - Classification of items into built-in (scientific and nonscientific) and movable (scientific and nonscientific).

Equipment Identification - Process of selecting the item, its specifications, manufacturer and model number but not designating the vendor.

Equipment Installation - The placement and connection of items in their designated location such that they are ready for turnover to the operational staff.

Equipment Life - The length of time an item is expected to perform satisfactorily when it receives scheduled maintenance and is operated by a properly trained individual.

Existing Equipment - Items that are on the property books of the host Governmental Facility.

External Support Services - Those functions that can be provided satisfactorily by a performer outside of the Facility.

Extrapolation - The extension of animal or other studies to potential effects on another species - especially man.

FDA - Food and Drug Administration.

FDCA - Food, Drug and Cosmetic Act.

FFA - Flammable Fabric Act.

FFDCA - Federal Food, Drug and Cosmetic Act (1938).

FHSA - Federal Hazardous Substances Act (1966). A statute defining some of the responsibilities of the Consumer Product Safety Commission (CPSC).

FID - Flame Ionization Detector.

FIFRA - Federal Insecticide, Fungicide and Rodenticide Act (1972).

FORSCOM - Forces Command.

FR - Federal Register. The official organ of the U.S. Government; published every working day.

Full Service Toxicology - Includes all 19 specifically identified toxicology tests, special scientific toxicology studies and genetic toxicology tests needed to meet Army's toxicology requirements and the tasks before, in parallel with and after toxicology testing.

FWPCA - Federal Water Pollution Control Act.

FY - Fiscal Year. The fiscal year of the U.S. Government is October 1 to September 30.

General Toxicology - Includes all testing that has lethality as an end point. In addition, it includes dermal irritation and sensitization and ocular irritation and metabolism and organic specific studies. It does not include oncogenic, behavioral, neurotoxicologic, mutagenic, reproductive or teratologic studies.

GLP - Good Laboratory Practices.

GOCO (Government-Owned, Contractor-Operated) - A function performed by contractor personnel in a Government-owned facility. Material and equipment may be furnished by the Government or acquired for the Government by the contractor.

GOGO (Government-Owned, Government-Operated) - A function performed by Government personnel in a Government-owned facility. Equipment may be owned or leased by the Government.

HEPA - High Efficiency, Particulate Air.

HHA - Health Hazard Assessment.

HMTA - Hazardous Materials Control Act (1975).

Hierarchical Testing - A progressive testing system which proceeds in increments of complexity, duration and cost based on several factors.

HSC - Health Services Command.

Hunter's Point - Navy's vacant Nuclear Biology Defense Laboratory.

HVAC - Heating, Ventilation and Air Conditioning.

In-house performance - The performance of CITA by Army military or Federal civilian personnel.

Inhalation Chamber - The enclosure and its connections used to house the laboratory animals during inhalation toxicology studies.

Inhalation Chamber System - The inhalation chamber and all supporting instrumentation, controls, test agent generators, air supply and exhaust air piping, filtration and conditioning equipment, and cages and racks required to expose laboratory animals for inhalation toxicology studies.

IPR - In-Process Review.

ITC - Interagency Testing Committee as established by Section 4 of TSCA.

LAIR - Letterman Army Institute of Research.

Lead Time - Time between start of the acquisition process and delivery of the item at its destination.

LSI - Life Systems, Inc.

MAM - Mission Area Manager.

MAP - Materiel Acquisition Process.

MENS - Mission Element Need Statements.

MIS - Management Information System.

Mutagenic testing - Testing to assess the potential hazard to human beings of a test substance due to interaction with genetic mechanisms with a resultant heritable change (mutation).

Mutagenicity - The induction of gene mutations.

NCI - National Cancer Institute.

NIEHS - National Institute of Environmental Health Sciences.

NIOSH - National Institute for Occupational Safety and Health.

Nonregulatory Requirements - Self-imposed requirements for toxicology testing, not regulated by law. Results from problems that are perceived or anticipated (carried out under implied requirements or for "moral" issues). These requirements may be reflected in Army regulations or DOD Directives. Meetings those requirements can improve combat effectiveness or reduce compensation and ligitation payments.

Nonscientific Equipment - Equipment needed in the Facility but not critical to laboratory experimental studies (such as office furniture and administrative equipment).

NTP - National Toxicology Program.

OMB - Office of Management and Budget.

OSHA - Occupational Safety and Health Act (Administration).

OTSG - Office of the Surgeon General

P/C Properties - The physical and chemical properties of a chemical substance.

Permanent Service - Functions essential to a Facility that will not be provided externally.

Pharmacokinetics - The science of determining the interrelationships of the chemicals on body metabolism and body metabolism on chemicals including the effect of time of exposure, dose, metabolism, excretion and related phenomena.

PL - Public Law.

PPPA - Poison Prevention Packaging Act.

Private commercial source - A private business, university, or other non-Federal activity located in the United States, its territories and possessions, or the Common wealth of Puerto Rico. This source is able to provide products or services required by the Government. States or State political subdivisions are considered private commercial sources.

Protocol - A detailed description of the design and technical conduct of a study e.g., procedures by which health effects tests are conducted.

QA - Quality Assurance.

QAU - Quality Assurance Unit.

QC - Quality Control.

Quality Assurance - A comprehensive system of plans, specifications and policies such as audits and inspections that are designed to ensure the collection, processing and reporting of data.

Quality Control - The system of activities designed to achieve and maintain a previously specified level of performance in data collection, processing and reporting.

Raw Data - Any laboratory worksheets, records, memoranda, notes, chromatograms or exact copies thereof, that are the results of original observations of a study.

RCRA - Resource Conservation and Recovery Act (1976).

RDT&E - Research, Development, Test & Engineering.

Redundancy - Backup items necessary to avoid loss of capability.

Regulation Requirements - Legally imposed toxicology testing, needed to conform to regulations. Criteria oriented with stated requirements. The protocols to be utilized are defined.

Reproductive effects - Impairment of reproduction.

RIF - Reduction in force.

San Francisco Bay Area - A 50 mile radius of the LAIR.

SAR - Structural Activity Relationship, the relationship between a chemical and its effects (biological, etc.) which form the basis for predicting effects based on structural relationships.

Scheduled Maintenance - Periodic servicing required to keep equipment functioning efficiently.

Scientific Equipment - Equipment required to perform laboratory experiments.

SDWA - Safe Drinking Water Act (1974).

SOP - Standard Operating Procedure.

Specimen - Any material derived from a test system for examination or analysis.

Standard - Levels established by a regulatory agency and used to determine compliance.

Startup - Time period starting with the acceptance date of the Facility and ending when the Facility achieves Operational Status.

STO - Science and Technology Objectives.

STOG - Science and Technology Objectives Guide.

Subchronic Tests - Tests of intermediate duration following continuous or repeated administration of a test substance over a period (typically 90 days). Used to determine effects or indications thereof without the longer time required for full-scale chronic effects tests.

Support Service - Those functions that can effectively be performed internally or externally to the Facility.

Support Service Contract - A situation wherein contractor personnel are on-site at a Government facility providing some degree of service or operation, but at which Government personnel are still working. A Support Service Contract could be as small as provisions of instrumentation maintenance and calibration or it could be complete research activities within the Government Facility but still under direction or operational control of Government managers.

Teratogenic - Potential of a test substance to produce defects in offspring resulting from prenatal exposure.

Teratogenicity - The induction of birth defects.

Test Article - A specific form of a chemical substance or mixture used to develop data (often used synonymously with Sample).

Test Facility - The establishment or organization actually conducts a non-clinical or toxicology study.

Test Mixture - A combination which results from mixing a test substance with another substance or substances (e.g., water, feed) for the purpose of exposing the test system.

Test System - The animal, microorganism or subpart thereof to which the test or control article is administered.

Tier Testing - See Hierarchical Testing.

Toxicology Method Development - Studies aimed at developing and/or validating new methods, procedures, protocols, etc. for toxicology testing purposes, including concomitant effects.

Toxicology or Toxic Effects or Hazards - For the study these terms are limited to the health effect aspects.

Toxicology Services or Toxicology Requirements - All tasks associated with toxicology from requirements identification through to completion of the toxicology activities associated with a specific requirement.

Toxicology Testing - Studies aimed at measuring the effects of chemicals in biological systems using established test protocols.

TRADOC - U.S. Army Training and Doctrine Command.

TSCA - The Toxic Substances Control Act (1976).

USAIDR - United States Army Institute of Dental Research.

USAISR - United States Army Institute of Surgical Research.

USAMBRDL - United States Army Medical Bioengineering Research & Development Laboratory.

USAMRDC - United States Army Medical Research and Development Command.

USAMRICD - United States Army Medical Research Institute of Chemical Defense.

USARIEM - United States Army Research Institute of Environmental Medicine.

USAMRIID - United States Army Medical Research Institute of Infectious Diseases.

USARL - United States Aeromedical Research Laboratory.

Unscheduled Maintenance - Service and repairs required because of an equipment failure or malfunction.

USDA - United States Department of Agriculture.

WRAIR - Walter Reed Army Institute of Research.

APPENDIX 2 TOXICOLOGY RELATED LAWS

TABLE A2-1 PUBLIC LAWS THAT REQUIRE TOXICOLOGY TESTING AND AFFECT TOXICOLOGY RESEARCH FACILITIES

Department	Agency/ Administration	Public Law Title	Acronym	Public Law and Amendments		Material or Scope of Work	Tox. Testing		Facility Compliance Requirements	
				Number	Date		Direct	Indirect	Direct	Indirect
—	EPA	Federal Insecticide, Fungicide, Rodenticide Act	FIFRA	92-516 94-140 95-396	10/21/72 11/28/75 9/30/78	Pesticides	X	—	X	—
—	EPA	Toxic Substances Control Act	TSCA	94-469	10/11/76	Hazardous and Toxic Substances	X	—	X	—
—	EPA	Resource Conservation and Recovery Act	RCRA	94-580 95-609 96-482	10/21/76 11/8/78 10/21/80	All Hazardous Materials	—	X	X	—
—	EPA	National Environmental Policy Act	NEPA	91-190 94-83	1/1/70 8/9/75	All Fed. Gov't. Activities	—	X	—	X
	EPA	Clean Water Act	CWA	92-500 95-217 95-576 96-483	10/18/72 12/27/77 11/2/78 10/21/80	Pesticides, Metals and Organics	—	—	—	X
—	EPA	Safe Drinking Water Act	SDWA	93-573 95-190 96-63 96-502	12/16/74 12/8/78 9/6/79 12/5/80	Pesticides, Metals and Organics	—	—	—	X
—	EPA	Clean Air Act	CAA	91-604 95-95	12/31/70 8/7/77	Particulates and Other Pollutants	—	—	—	X
DOL	OSHA	Occupational Safety and Health Act	OSHA	91-596	12/29/70	Workplace Hazards	—	X	X	—
USDA	—	Animal Welfare Act	AWA	89-544 91-579 94-279	8/24/66 12/24/70 4/22/76	Animals	—	—	X	—
DHHS[a]	FDA	Federal Food, Drug and Cosmetic Act	FFDCA	52-1040	6/25/38	Foods, Drugs and Cosmetics	X	—	X	—
DHHS	FDA	Public Health Service Act	PHSA	58-682	7/1/44	Biological Products	—	X	—	X
—	CPSC	Consumer Product Safety Act	CPSA	92-573 94-284 95-319 95-631	10/27/72 5/11/76 7/11/78 11/10/78	Consumer Products	X	—	—	—
—	CPSC	Federal Hazardous Substances Act	FHSA	86-613 95-631	7/12/60 11/10/78	Consumer Products	—	X	—	X
DOT	MTB	Hazardous Materials Transportation Act	HMTA	93-633	1/3/75	Explosives, Pesticides and Organics	X	—	X	—
DOE	NRC	Atomic Energy Act	AEA	83-703	8/30/54	Radioactive Compounds	—	—	X	—

(a) Department of Health and Human Services, formerly Department of Health, Education and Welfare

TABLE A2-2 SIGNIFICANT EXECUTIVE ORDERS RELATING TO TOXICOLOGY TESTING

Executive Order Title	Number	Date	Scope of Document
Federal Compliance with Pollution Control Standards	12088	10/13/78	Requires Federal depts. comply with both substantive and procedural aspects of all Federal environmental legislation (TSCA, FIFRA, CAA, CWA, etc.)
Occupational Safety and Health Programs for Federal Employees	12196	2/26/80	Extends OSHA-type protection to Federal employees

TABLE A2-3 THE ARMY ENCOUNTERING FOREIGN TOXIC SUBSTANCES LAW

Country	Law or Proposal (1978 Data)	Date Proposed or Passed
Australia	Proposal	1977
Canada	Law	1975
France	Law	1977
Japan	Law	1973
Norway	Law	1976
Sweden	Law	1973
Switzerland	Law	1969
W. Germany	Proposal	1978
United Kingdom	Proposal	1977
United States	Law	1976

Source: Dow Chemical

AD-A114 613 LIFE SYSTEMS INC CLEVELAND OH F/G 6/20
MAMMALIAN TOXICOLOGY TESTING: PROBLEM DEFINITION STUDY. PART 1.--ETC(U)
MAR 81 R A WYNVEEN, R H REUTER, R J DAVENPORT DAMD17-81-C-1013
UNCLASSIFIED LSI-TR-477-2 NL

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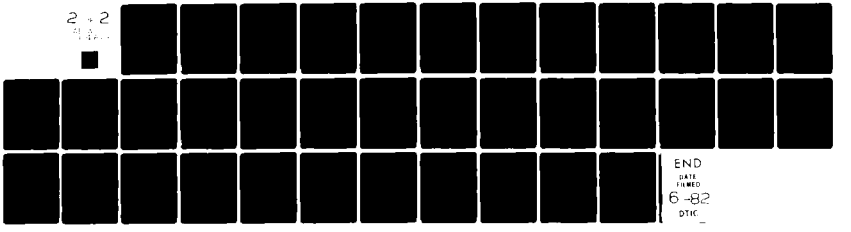

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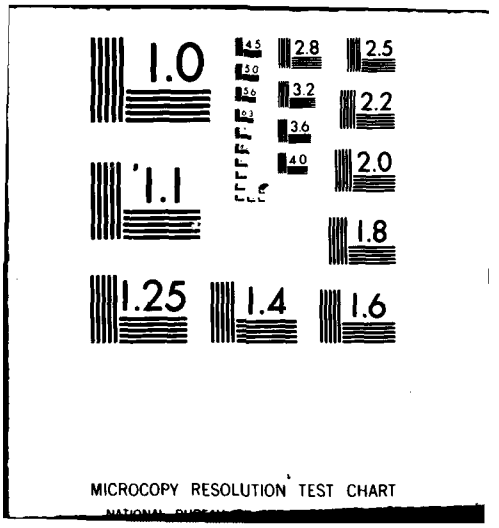
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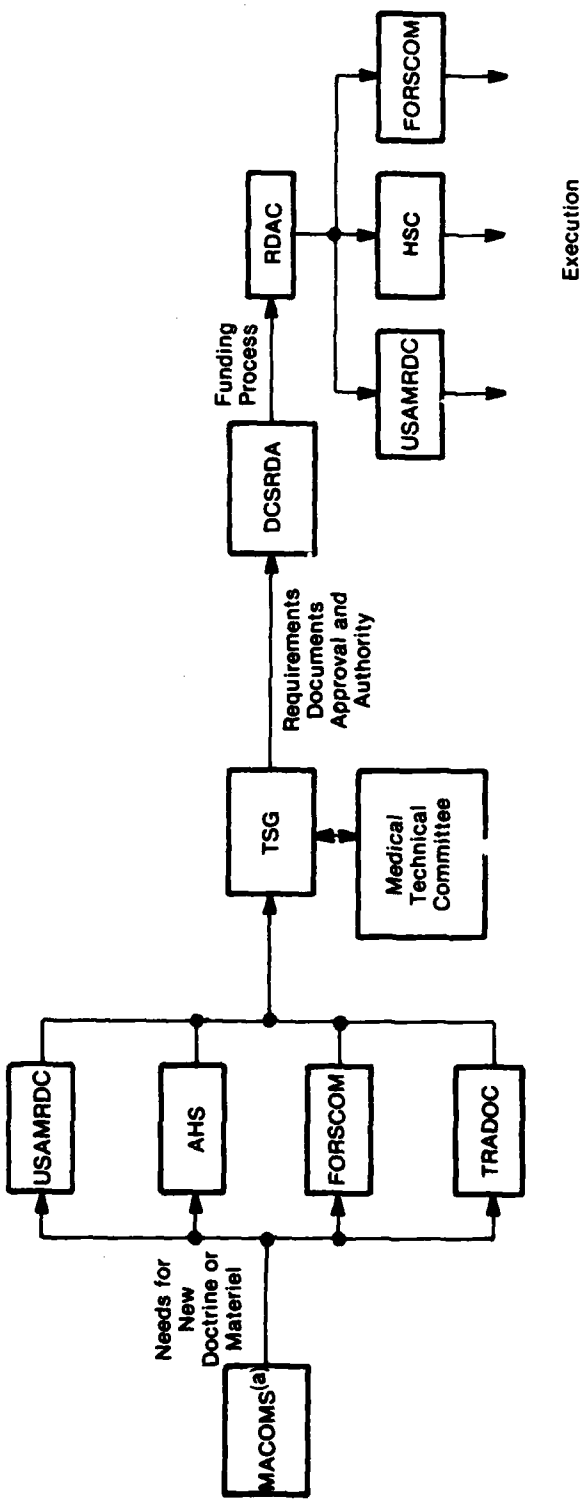
MICROCOPY RESOLUTION TEST CHART

APPENDIX 3 REQUIREMENTS INTERFACES



(a) Also included are Navy and Air Force needs, if appropriate

FIGURE A3-1 REQUIREMENTS DEVELOPMENT FOR MEDICAL MATERIEL

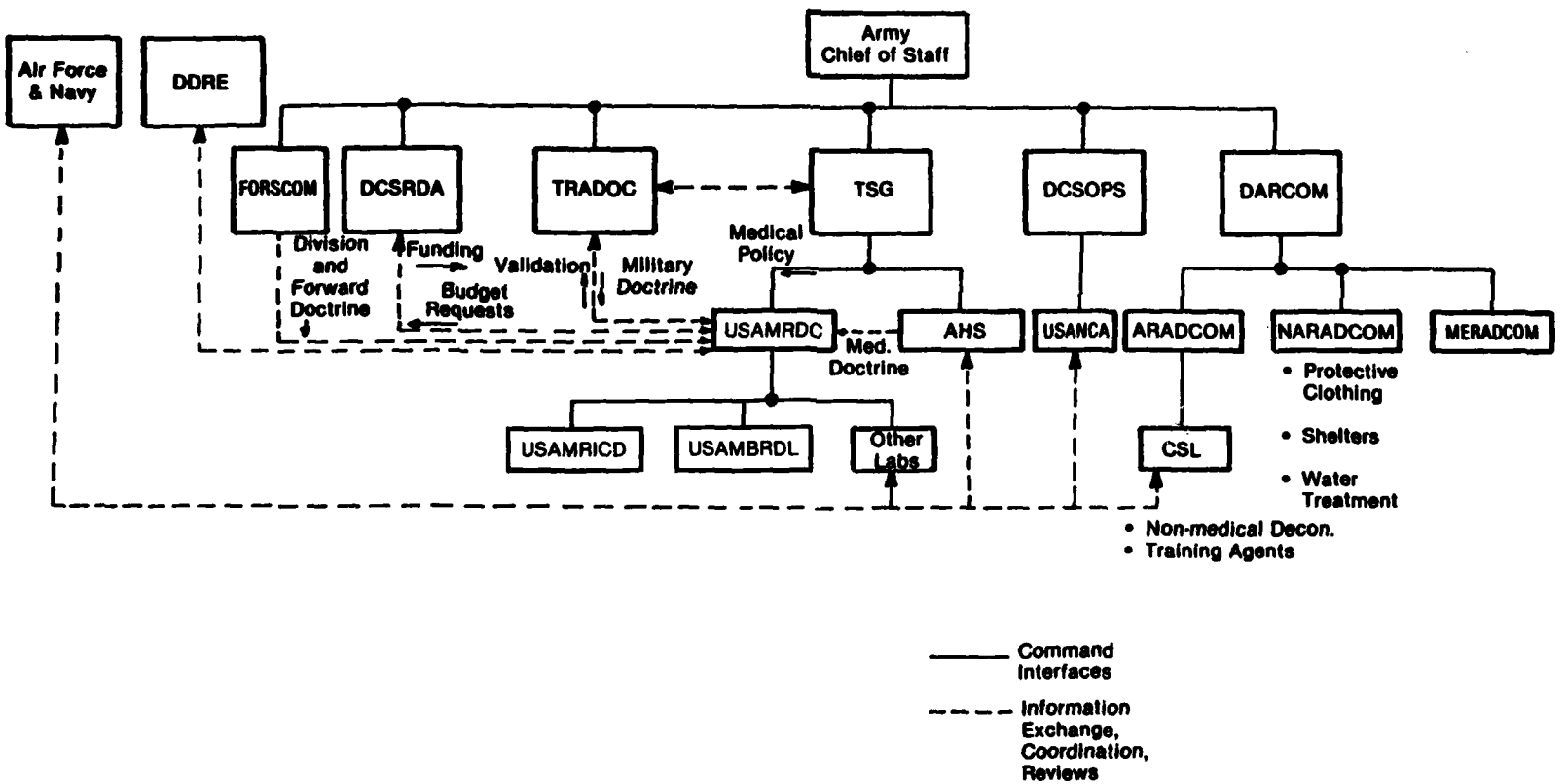
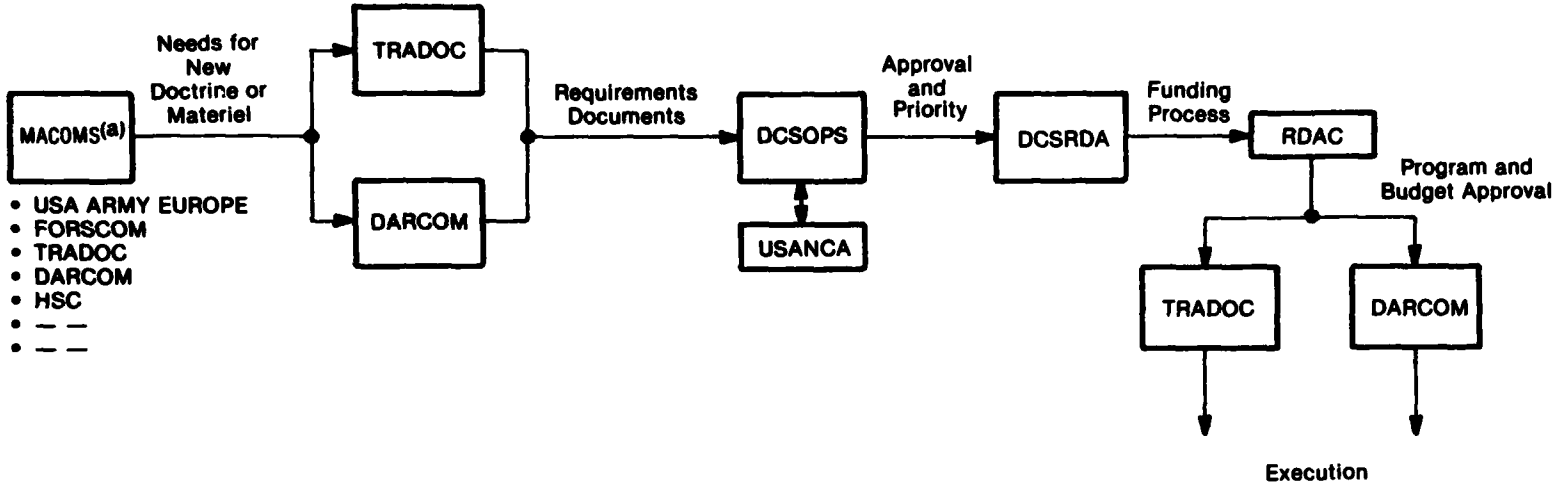


FIGURE A3-2 MAJOR IDENTIFIED INTERFACES WITHIN A MEDICALLY RELATED PROGRAM, E.G., CHEMICAL DEFENSE



(a) Also included are Navy and Air Force needs, if appropriate

FIGURE A3-3 REQUIREMENTS DEVELOPMENT FOR NONMEDICAL MATERIEL

APPENDIX 4 TYPICAL ONGOING TASKS PROVIDED BY A FULL-SERVICE FACILITY

Before Testing

1. Monitor and maintain knowledge of toxicology testing capabilities available to fulfill medical and non-medical military needs.
2. Perform continuing analyses of military user (e.g., FORSCOM) needs for toxicology testing.
3. Identify waste products from munitions, synthetic fuels, etc.
4. Determine and maintain priority setting mechanisms to select the most important chemicals for tests.
5. Prepare and maintain long range R&D Plan (per AR 70-55 (paragraph 9b) and AR 70-1 (paragraph 1-8b)).
6. Provide expertise to evaluate specific toxicology research testing requirements for the USAMRDC on a continuing basis.
7. Review health records on exposed populations. This would include morbidity and mortality reports.
8. Perform measurements on suspected exposed population and compare with control group. This could include both prospective and retrospective studies.
9. Identify potentially toxic materials (chemicals).
10. Provide advice/recommendations on toxicology testing needs.
11. Perform literature and information reviews/searches (to minimize toxicology testing needs).
12. Basic research on toxicology testing (to develop techniques to extrapolate more effectively from animal data to humans).
13. Assess scientific data bases that can define cost-effective procedure for evaluating the toxic environmental hazard of Army wastes and for complying with waste treatment and disposal requirements.
14. Define improved methods for evaluating animal test data and making species extrapolations to humans for predicting toxic substance effects on troops under military training/combat conditions.
15. Define sensitive and cost effective test procedures for evaluation of organ specific toxicity.
16. Complete short-term *in vivo* tests predictive of oncogenic potential of chemicals and chemical mixtures for use in assessing military toxic hazards within time and cost constraints.

17. Prepare for sensitive and relevant behavioral tests for prediction of human performance decrement from toxic substance exposure of troops under training/combat conditions.

18. Define improved toxicologic test procedures for predicting toxic substance effects on troops exposed under realistic field training/combat conditions.

19. Define improved sensitive test systems for evaluating and predicting the interactive effects of toxic substances and other stresses on troops under realistic field exposure conditions.

20. Conceive of short-term test procedures for evaluating Army relevant environmental pollutants with reduced time and cost requirements.

21. Complete chemical and physical characterization tests on potentially toxic materials and environments - so they can be simulated in the laboratory to obtain the toxicology data.

<u>During Testing</u>

22. Toxicology Testing (Limited Scope, Tier 1).

23. Toxicology Testing (Medium Scope, Tier 2).

24. Toxicology Testing (Full Scope, Tier 3).

<u>In Parallel with Testing</u>

25. Assemble toxicology data-base for parallel efforts (toxicologic and/or epidemiologic studies).

26. Maintain status reporting during materiel development cycle.

27. Provide inputs needed for regulatory affairs.

28. Provide training of Army personnel in toxicology technology and application of results to materiel development.

<u>After Testing</u>

29. Establish criteria to avoid reversible toxic effects.

30. Establish criteria to avoid irreversible toxic effects.

31. Establish sensitive and cost-effective procedures for evaluating Army relevant environmental pollutants to recommend environmental quality protection criteria.

APPENDIX 5 SERVICES THAT COULD BE PROVIDED FOR EACH ASSIGNMENT

1. Review materiel/equipment test plans and design concepts.
2. Evaluate range of scenarios for exposure to toxic materials (a chemical or mixture of chemicals).
3. Alert DA to requirements.
4. Alert DA to areas of vulnerability.
5. Recommend course(s) of action.
6. Respond to requests to do work;
   a. Get facts, report back.
   b. Expand involvement.
7. Take action needed.
8. Indicate when toxicological data inputs required.
9. Prepare literature review on health effects of exposures (including, where applicable, all material projected for use in the manufacturing process to determine work completed by others).
10. Complete Problem Definition Studies.
11. Evaluate literature on health effects for given type(s) of exposures.
12. Determine applicability of existing protocols to military unique exposures.
13. Complete production process evaluation studies - specific chemicals, exposures.
14. Make risk assessment analysis (Health/Environmental).
15. Make toxicology's input to health hazard assessment analysis.
16. Recommend concepts for protection against hazard(s).
17. Recommend materials for protection against hazards.
18. Identify specific testing requirements.
19. Identify specific research requirements.
20. Select methodology and have it reviewed by peer groups.
21. Establish applicability of animal models to military unique exposures to hazard requirement. Determine best animal models for various chemical tests (this could be considered part of the protocol preparation).

22. Carry out epidemiology studies.

23. Determine priority and decision on testing.

24. Chemically (analytically) characterize potentially toxic materials or environments -- so they can be simulated in the laboratory to obtain the toxicology data. Chemistry literature review to:

    a. Determine anticipated products
    b. Develop capability to characterize (sampling, analytical approaches, etc.):

        1. Laboratory.
        2. Field.

    c. Do analysis.
    d. Determine how to duplicate for mammalian toxicology testing.

25. Physical (chemical) aspects of:

    a. Physical form (gas, liquid, solid).
    b. Chemical specie (e.g., valence state of metal).
    c. Route(s) of exposure.
    d. Magnitude of concentration peak.
    e. Duration of exposure.
    f. Frequency of exposure.
    g. Intervals between exposures.

26. Physically characterize the form of chemicals, e.g., particle size and distribution of a smoke.

27. Develop chemical generation simulators to allow reproduction of chemical and physical characteristics in the toxicology laboratory.

28. Develop exposure equipment that will enable the tests to duplicate the exposure levels, duration and multiple stresses.

29. Measure actual industrial environment characteristics.

30. Characterize soldier's field operating environments.

31. Make in-plant and in-field measurements over time with variations in raw material, production processes that produce the material, standard levels of maintenance of equipment, operation under different climatic conditions such as temperature, humidity which may impact by-product formation rate or acutal formation, etc.

32. Identify new toxicity tests/protocols needed.

33. Develop methodology and indicate data inputs required.

34. Decide on route(s) of exposure.

35. Complete clinical studies.

36. Establish test methodology. (Prepare protocols and analytical chemical procedures prior to "production type" research/testing.)

37. Weigh the importance of data inputs.

38. Synthesis chemicals needed.

39. Validate new toxicity tests/protocols.

40. Measure toxicology through proper conduct of required studies.

41. Complete selected toxicology evaluation studies (General Toxicology, ..., Behavioral)

42. Convert new toxicity tests/protocols to standards.

43. Complete comparative metabolism studies.

44. Establish dose-response relationship for all identified end points.

45. Apply safety factors.

46. Complete inter- and intra-species extrapolation and low to high concentration levels extrapolation.

47. Identify and recommend protection required.

48. Provide guidance for the Surgeon General and TRADOC users.

49. Identify interactive mechanisms.

50. Establish environmental quality protection criteria recommendations.

51. Recommend criteria communication methods.

52. Establish criteria to avoid reversible toxic effects.

53. Establish criteria to avoid irreversible toxic effects.

54. Recommend occupational health protection criteria.

55. Recommend occupational health exposure limits.

56. Transfer technology to literature, other users, etc.

57. Recommend surveillance techniques.

58. Recommend process waste treatment procedures.

59. Identify modifications of soldier capabilities in using materiel.

60. Expand toxicology portion of program's Health Hazard Assessment data base.

61. Complete retrospective epidemiology studies.

62. Complete re-evaluation of standards.

APPENDIX 6 STUDY PROGRAM CONSTRAINTS

Mammoth Size of Job:

1. Army's a $40 Billion/Yr. Organization
2. Army's in J10 Industries
3. Army Constantly Changes, No Common Data Base Dateline

Time Frame Short:

1. 3½ Months, 60 Working Days to Reach Final Reports
2. Delivery Slow of Supporting Documents

Poor Available Data Bases:

1. Scattered All Over
2. Buried In Files
3. Imaginary, Doesn't Exist
4. Classified Content Unknown
5. No USAMRDC Lab/Mission Area Manager Interfaces

Many Guidelines Missing:

1. Budget Level for Added Capacity
2. Who Decision Makers Are
3. Personnel Slots Approximate Number of

Many Unknowns Exist

1. Who Sets Priorities?
2. What's Current Capability?
3. What's Current Capacity?
4. Organizational Boundaries?
   a. TSG/DARCOM?
   b. USAMRDC/HSC?
   c. USAMRDC/Labs (9)
   d. Labs/MAMs?
   e. Applied/Basic Research

Addition to Scope, "Changes":

1. Add Second GOCO Model Site (after proposal)
2. Expand Production Testing to Include Applied Research (5% into Schedule)
3. USAMRDC Restricts Staff (30% into Schedule)
4. Add Classified Clearance (60% into Schedule)
5. Add Genetic Toxicology Testing (70% into Schedule)
6. Expand Summary for Broader Audience (95% into Schedule)

Scope Varied and Complex:

1. Testing Versus Full Service
2. Many Misconceptions Exist on Terminology
3. Determine Number/Type of Weapons, e.g., Main Battlefield Tanks
4. Determine Costs of Toxicology Facility
5. Equip an Inhalation Facility
6. Identify Foreign Toxicology Labs

APPENDIX 7 TYPES OF TOXICOLOGY TESTS

INTRODUCTION

Three types of toxicology tests were identified to meet the USAMRDC requirements:

1. General Toxicology Tests
2. Genetic Toxicology Tests
3. Special Scientific Toxicology Tests (Studies)[a]

General Toxicology Tests

Table A7-1 presents a list of 19 types of Army required mammalian general toxicology tests. Information on each test includes duration, type of animal, route of exposure and outcome, usually "general toxicology." The latter includes lethality, metabolism/pharmacokinetics and portions of special toxicology disciplines such as pharmacodynamics. Only portions of the latter are included, however, so as not be be confused with the similiar but full scale, special scientific studies. Also, General Toxicology, as used in this context, includes the dermal irritation and sensitization and ocular irritation outcomes.

The list of 19 tests resulted from a survey of all known types of mammalian toxicology tests descriptors and which than was reduced to a list of those most likely to be applicable to the Army's requirements. This was followed by an identification of specific test protocols for the group of 19.

To accomplish all the USAMRDC's mammalian toxicology research needs required that various special scientific toxicology studies be incorporated in additon to the general toxicology and neurotoxicology tests (Table A7-1).

Genetic Toxicology Tests

Considerable advances in technology are being made to minimize the cost of toxicology testing. A portion of these efforts involve genetic toxicology tests. The program identified five major genetic toxicology test categories:

1. Standards for detecting gene mutations.
2. Standards for detecting heritable chromosomal mutations.
3. Standards for detecting DNA repair or recombination as an indicator of genetic damage.
4. Standards for detecting chromosomal damage.
5. Standards for detecting DNA alkylation.

These five tests categories are further defined in Table A7-2.

It is the Army's decision as to which of the genetic toxicology tests be incorporated into the Facility's capability. It is recommended that many of

(a) For the remainder of the report, the special scientific toxicology tests will be referred to as studies. This is done to reflect the more research oriented aspect of the activities.

TABLE A7-1 SPECIFIC TYPES OF ARMY MAMMALIAN TOXICOLOGY TESTS

No.	Duration		Type of Animal	Route of Exposure	No. of Species	Outcome[a,b]
	General	Specific				
1.	Acute	Short	Rodent	Oral	1	General Toxicology
2.	Subchronic	90-Day	Rodent	Oral	1	General Toxicology
3.	Chronic	Life-Time	Rodent	Oral	1	General Toxicology
4.	Acute	Short	Rodent	Inhalation	1	General Toxicology
5.	Subchronic	X-Day	Rodent	Inhalation	1	General Toxicology
6.	Chronic	Life-Time	Rodent	Inhalation	1	General Toxicology
7.	Acute	Short	Primate	Inhalation	1	General Toxicology
8.	Subchronic	90-Day	Primate	Inhalation	1	General Toxicology
9.	Chronic	Life-Time	Primate	Inhalation	1	General Toxicology
10.	Subchronic	90-Day	Dog	Oral	1	General Toxicology
11.	Acute	Short	Rabbit	Dermal	1	General Toxicology
12.	Subchronic	Z-Day	Rabbit	Dermal	1	General Toxicology
13.	Acute	Short	Rabbit	Ocular	1	General Toxicology
14.	Acute	≥21 day	Chicken	Oral	1	Neurotoxicity
15.	Subchronic	90-day	Chicken	Oral	1	Neurotoxicity
16.	Acute	Short	Rabbit	Dermal	1	Irritation
17.	Subchronic	90-day	Rabbit	Dermal	1	Irritation
18.	Acute	Z-Day	Rabbit	Ocular	1	Irritation
19.	Acute	Short	Rodent[c]	Dermal	1	Sensitization

(a) Efficacy would be included for drugs and vaccines.
(b) General toxicology includes lethality and metabolism/pharmacokinetics plus minor investigations of the several other toxicology disciplines (e.g., pharmacodynamics).
(c) Guinea Pig

TABLE A7-2 GENETIC TOXICOLOGY TEST PRICES

	Price, $(000)[a]
A. Standards for Detecting Gene Mutations	
1. Detection of Gene Mutations in Bacteria	
a. The Salmonella/Microsomal Assay	1.0
b. The Escherichia coli WP2 and WP2 *uvrA* Reverse Mutation Assay	1.0
2. Detection of Gene Mutations in Eukaryotic Microorganisms	
a. Aspergillus nidulans	1.0
b. Neurospora crassa	1.0
3. Detection of Gene Mutations in Insects	
a. Drosophila melanogaster Sex-Linked Recessive Lethal Test	7.0
4. Detection of Gene Mutations in Somatic Cells in Culture	
a. Mammalian Cell Culture — L5178Y Mouse Lymphoma Cells	4.5
b. Mammalian Cell Culture — V79 Chinese Hamster Cells	4.5
c. Mammalian Cell Culture — Chinese Hamster Ovaryl (CHO) Cells	4.5
5. Detection of Gene Mutations in Mammals	
a. The Mouse Specific Locus Test	40.0
B. Standards for Detecting Heritable Chromosomal Mutations	
1. *In Vivo Cytogentics Test in Mammals*	13.0
2. Detection of Heritable Chromosomal Damage in Insects	
a. Chromosomal Damage in Drosophila melanogaster	14.0
3. The Dominant Lethal Test in Mammals	15.0
4. The Heritable Translocation Assay	30.0
C. Standards for Detecting DNA Repair or Recombination as an Indicator of Genetic Damage	
1. Detection of Genetic Damage in Bacterial by DNA Repair	0.6
2. Unscheduled DNA Synthesis in Mammalian Cells in Culture	2.5
3. Detection of Mitotic Crossing Over and/or Gene Conversion in Yeast	5.0
4. Sister Chromatid Exchange in Mammalian Cells in Culture	2.5
D. Standards for Detecting Chromosomal Damage	
1. In Vitro Cytogenetics Assay	0.7[b]
2. Micronucleus Assay	2.2[b]
E. Standards for Detecting DNA Alkylation	
1. DNA Alkylation in Drosophila melanogaster Sperm Cells	10.0[b]
2. DNA Alkylation in Rodent Sperm Cells	10.0[b]
3. DNA Alkylation in Mammalian Cells in Culture	5.0[b]

(a) SOURCE: "Cost Analysis Methodology & Protocol Est. TSCA Health Standards & FIFRA," Enviro Control April 3, 1981, except for those noted (b)
(b) SOURCE: Price Quotation from Litton-Bionetics, Dr. D. Brusick, March, 1981.

the in vitro tests be included (Module 62). The in vivo genetic toxicology studies, can be incorporated through the addition of Module 63 or, with some rearrangement, through one of the oral exposure areas (e.g., Modules 1 through 3, acute, subchronic and chronic oral exposure areas for rodents, respectively).

Special Scientific Toxicology Studies

The toxicology capability envisioned as able to be incorporated into the Facility include the following:

1. Behavioral Studies
2. Metabolism/Pharmacokinetic Studies
3. Pharmacodynamic Studies
4. Oncogenic Studies
5. Respiratory Physiology Studies
6. Reproduction Studies
7. Teratology Studies
8. Neurotoxicity Studies

These are in addition to the General Toxicology tests cited above.

Of these, it is recommended the Facility provide the specific special toxicity studies noted at the right hand side of Table A7-3 including the combined protocols of (a) general toxicity and oncogenic studies and (b) reproduction and teratology studies. These include, for example, behavioral toxicity studies by the inhalation route of exposure with rodents and primates.

Table A7-2 and A7-3 list the prices established for the various mammalian toxicology tests where they could be done on a contracted basis. Obtaining accurate pricing information for toxicology testing is very difficult. This occurs because of the inconsistencies in protocols, interpretation of protocols, depth with which the personnel providing pricing information view the assignment, etc. The table is included, however, more to reflect the breakout of tests the Facility should perform to meet Army requirements than the price for the test. The background discussions on the latter are contained in a Study file Memo.

Tests Actually Selected

A specific selection of which capabilities/mammalian toxicology tests should be done within the Facility depends upon decisions made concerning:

1. The control the Army desires over the implementation of each test;
2. The level of funding it desires to invest in establishing the Facility, its capability and capacity; and
3. The success experienced in identifying the level of test volume, urgency and timing for providing the capability.

A major driver will be the number of times per year (volume) the particular test is ultimately determined to be required, the funding provided by the Facility users and, possibly, the sharing of the Facility capabilities with other organizations. The latter includes the Air Force and Navy, and other Federal Agencies such as the National Cancer Institute or other National Toxicology Program participating agencies.

TABLE A7-3 MAMMALIAN TOXICOLOGY TEST PRICE LIST (3/8/81)

Test No.	Duration	Type of Animal	Route of Exposure	Price, $(000) Per Outcome[a]							
					Special Scientific Toxicology Studies[b]						
										Combined Protocols	
				General Toxicology[b]	Behavioral	Onco-genic	Repro-duction	Terato-genic	Neuro-toxi-cology	Gen. Tox. + Oncog.	Repro./ Terato.
1	Acute	Rodent[d]	Oral	2.4[e]	—	—	—	—	—	—	—
2	Subchronic	Rodent[d]	Oral	56[e]	—	—	—	—	—	—	—
3	Chronic	Rodent[d]	Oral	495[e]	—	377[e]	114[e]	27[e]	—	600[f]	125[f]
4	Acute	Rodent[d]	Inhalation	5.0[e]	—	—	—	—	—	—	—
5	Subchronic	Rodent[d]	Inhalation	64[e]	100[f]	—	—	—	—	—	—
6	Chronic	Rodent[d]	Inhalation	613[e]	—	515[f]	—	—	—	1000[f]	—
7	Acute	Primate	Inhalation	39[f]	—	—	—	—	—	—	—
8	Subchronic	Primate	Inhalation	196[f]	150[f]	—	—	—	—	—	—
9	Chronic	Primate	Inhalation	518[f]	—	420[f]	—	—	—	800[f]	—
10	Subchronic	Dog	Oral	104[e]	—	—	—	—	—	—	—
11	Acute	Rabbit	Dermal	4.2[e]	—	—	—	—	—	—	—
12	Subchronic	Rabbit	Dermal	75[g]	—	—	—	—	—	—	—
13	Acute	Rabbit	Ocular	2.5[f]	—	—	—	—	—	—	—
14	Acute	Chicken	Oral	—	—	—	—	—	5.4[e]	—	—
15	Subchronic	Chicken	Oral	—	—	—	—	—	20[e]	—	—
				Irritation	Sensitization						
16	Acute	Rabbit	Dermal	0.7[e]	—						
17	Subchronic	Rabbit	Dermal	3.0[g]	—						
18	Acute	Rabbit	Ocular	0.9[e]	—						
19	Acute	Guinea Pig	Dermal	—	3.9[e]						

(a) Rounded off to nearest $1,000 for prices in excess of $5,000. Assumes one species.
(b) Special Scientific Toxicology Studies: Metabolism/Pharmacokinetics, Pharmacodynamics, and Respiratory are deleted since they are not a part of the 19 tests.
(c) General Toxicology includes lethality, metabolism and pharmacokinetics/pharmocodynamics.
(d) Rodent studies price was based on use of the rat.
(e) SOURCE: *Enviro Control, Inc.* 1980, *Cost Analysis Methodology & Protocol Estimates. TSCA Health Standards and FIFRA Guidelines.* Rockville, MD: Enviro Control, Inc. U.S. Environmental Protection Agency.
(f) Price estimated by LSI since no quotable source was identified.
(g) SOURCE: ICF, Inc. 1980. *Profile of the Chemical Safety Testing Industry: An Assessment of Pesticide Testing Capacity. Final Report.* Washington, DC: ICF, Inc. U.S. Environmental Protection Agency.

IMPLEMENTING SELECTED CAPABILITY AT THE FACILITY

As was noted, the specific tests and toxicology related activities/tasks incorporated must be determined by the Army. It is envisioned, however, that the selected capability should be implemented in two stages. Further, each stage should be built up incrementally (Life Systems, Inc. 1981a).

APPENDIX 8 CURRENT AND POTENTIAL TOXICOLOGY INPUTS TO LIFE CYCLE MANAGEMENT OF DARCOM MATERIEL

The following pages contain:

The former provides a list of documents from the DARCOM life cycle management process while the Study found to be likely candidates for making toxicology inputs. The latter illustrates where the current first one of two input is made in the management network.

TABLE A8-1 CURRENT AND POTENTIAL TOXICOLOGY INPUTS TO LIFE CYCLE MANAGEMENT TO DARCOM MATERIEL

Acronym	Description	Life Cycle Network Block: Conceptual 100	Validation 200	Validation 300	Full Scale Devel. 400	Full Scale Devel. 500	Production 600	Production 700	Operational & Disposal 800	Operational & Disposal 900
BTA	Best Technical Approach	146		371						
CDRL	Contractor's Data Requirements List	131	256		442		604			
	Certification for Release							791		
	Conformance to Rule of International Law	161		323						
COSIS	Care of Supplies in Storage								853	
	Critical Issues	126			467					
	Depot Maintenance					569,570 571	653,654			
	Design Review		288		485					
	Development Estimate	117	252		483					
DRA	Decision Risk Analysis	168		366		583		721		
EIA/EIS	Environmental Impact Assessment/Statement	157			461					
EIALC	Environmental Impact Assessment for Life Cycle	116		317						951
	Environment	116,157		317	461					951
FOE	Follow-on Evaluation								803	
	Health Hazard	158[a]		318[a]		529				
IPR	In-Process Review	188		377		523,527 590				
LCMM	Life Cycle Management Model									
LCM	Life Cycle Management Planning	111								
MIDP	Major Item Distribution Plan				496			771	873	
MM&T	Manufacturing Methods & Technology			361						
MOS	Military Occupational Specialty		236		429	566		746		
MTP	Manufacturing Technology Program			358						
OT	Operational Test			338		546	697			
OTP	Outline Test Plan	117,178	278,282	348,351	473,475	552,553	622,623	793		
PEP	Producible Engineering & Planning			354		533				
PQT	Prototype Qualification Test					526,527 528				
RAM	Reliability, Availability & Mantainability		206		404		694			
ROC	Required Operational Characteristics		292	368						
	Safety Release			322		530	682			
	Safety Statement			321		529	681			
SEAR	Summary Engineering Assessment Report					544				
	System Assessment								833	
TDP	Test Design Plan	176	277,283	347	472,476	551	621,624	794		
	Transportation		242		434	532,568		756		

(a) Current input points

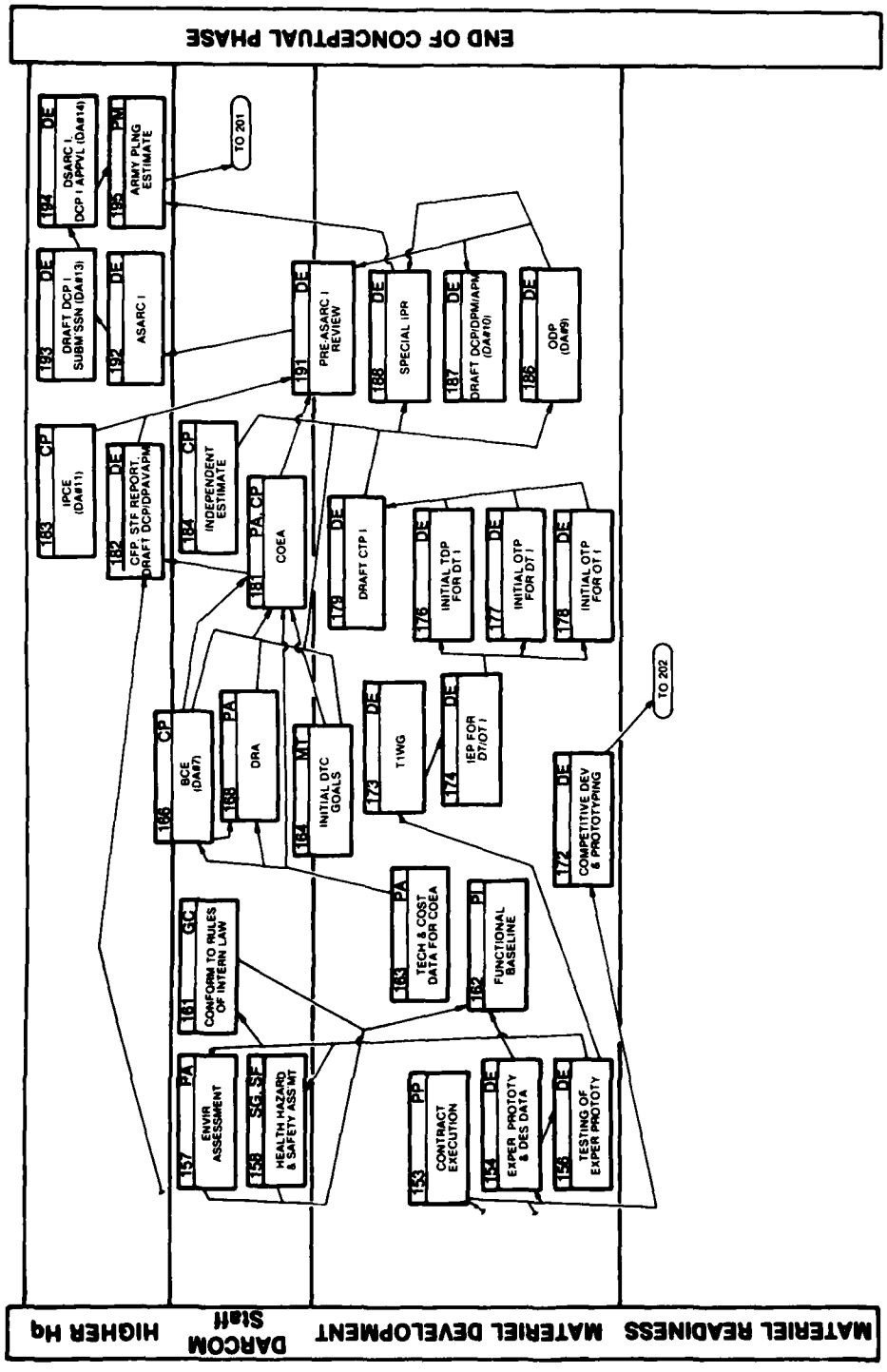


FIGURE A8-1 SECTION OF MATERIEL LIFE CYCLE MANAGEMENT NETWORK

APPENDIX 9 CHEMICAL USES AND CHEMICALS

Chemical Use	Types	Types of Types	Foreign Mat'l.	No. Cmpds. 1	2	X	Inter-mediate	Degradation Products Mfctr.	Uses	Spills
Agents	7	34		X	-	-	Several	X	X	X
Clothing	10	38(a)		X	?	-	--	X	X	X
Drugs/Vaccines	7	21(a)		X	-	-	Several	-	X	-
Explosives	12	1,320		X	X	(b)	Several	-	X	X
Fabric Treatments	4	8(a)		X	X	?	--	X	X	X
Fuels	5(a)	5s		X	?	?	--	-	X	X
Fuel Additives	7	29		X	X	?	Several	X	X	X
Preservatives	4	8(a)		X	?	-	--	X	X	X
Propellants	7	17		(c)	(d)	(e)	Several	X	X	X
Smokes & Obscurants	10	72(a)		X	X	X	Several	X	X	X
Synthetic Fuels	4	13(a)		X	X	?	Several	X	X	X
Others										
Cosmetics	5(a)	10(a)		X	X	?	--	-	X	-
Dyes	5(a)	10(a)		X	-	-	Several	-	-	X
Fungicides	5(a)	10(a)		X	-	-	--	X	X	X
Germicides	3(a)	6(a)		X	-	-	--	X	X	X
Herbicides	5(a)	10(a)		X	-	-	--	X	X	X
Insecticides	5(a)	10(a)		X	-	-	--	X	X	X
Lubricants	5(a)	10(a)		X	X	?	--	-	X	X
Pesticides	5(a)	10(a)		X	-	-	--	X	X	X
Plating	10(a)	10(a)		X	X	?	--	-	X	X
Rodenticides	5(a)	10(a)		X	-	-	--	X	X	X
Soaps/Detergents	5(a)	10(a)		X	-	-	--	X	X	X
Solvents	10(a)	20(a)		X	?	-	Several	X	X	X
Totals	145	1,691(a)								
	7	21								
	7	34+								
	131(a)	1,636								

(a) An estimated number versus the types of types found during the study and presented elsewhere (Life Systems, Inc. 1981c).
(b) Gelatinizing Agent, Waterproofing Agent, Priming Composition
(c) Oxidizer
(d) Reducer
(e) Stabilizer

SUPPORTING INFORMATION ON CHEMICAL USES AND CHEMICALS

		Types of Types
Agent Types		
1.	Blister	8
2.	Blood	2
3.	Choking	1
4.	Incapacitating, Central Nervous System Depressants	14
5.	Incapacitating, Central Nervous System Stimulants	2
6.	Nerve	5
7.	Riot Control	2(a)
	Total	34
Clothing Types		
1.	Body Armor	2(a)
2.	Coveralls	5(a)
3.	Face Nets	2(a)
4.	Gloves	3(a)
5.	Goggles	5(a)
6.	Helmets	3(e)
7.	Masks	5(a)
8.	Shoes	5(a)
9.	Socks	5(a)
10.	Spectacles	3(a)
	Total	38(a)
Drugs/Vaccines		
1.	Antiradiation	3(a)
2.	Antishock	3(a)
3.	Bacterial	5(a)
4.	Infection Prevension	3(a)
5.	Parasitic	2
6.	Rickettsia	1
7.	Viral	4
	Total	21(a)
Explosive Types		
1.	Anti-aircraft Guns	2(a)
2.	Bombs	2
3.	Bullets	100(a)
4.	Detonating Cords	10(a)
5.	Detonators	10(a)
6.	Fuses & Components	1,100
7.	Grenades	5
8.	Missiles	24
9.	Plastics	5(a)
10.	Primers	10(a)
11.	Projectiles	50(a)
12.	Pyrotechnics	2(a)
	Total	1,320(a)

Support Information on Chemical Uses and Chemicals - continued

		Types of Types
Fabric Treatment		
1. Durable Press		2(a)
2. Fire Retardants		2(a)
3. Oil Repellants		2(a)
4. Water Repellants		2(a)
	Total	8(a)
Fuels		
1. Aircraft		1(a)
2. Armored Vehicle		1(a)
3. Diesel		1(a)
4. ?		1(a)
5. ?		1(a)
	Total	5(a)
Fuel Additives Types		
1. Antioxidants		5(a)
2. Biocides		5(a)
3. Corrosion Inhibitors		5(a)
4. Fire Control		3(a)
5. Icing Inhibitors		3(a)
6. Lubricity Improvers		5(a)
7. Static Dissipators		3(a)
	Total	29(a)
Preservatives		
1. Cloth		2(a)
2. Leather		2(a)
3. Structural		2(a)
4. Wood		2(a)
	Total	8(a)
Propellant Types		
1. Biopropellant		4(a)
2. Fast Burning		2(a)
3. Monopropellants		2(a)
4. Other Additives		3(a)
5. Smokeless		3(a)
6. Stabilizer		2(a)
7. Ultrafast Burning		1(a)
	Total	17(a)
Smokes & Obscurants		
1. Infrared Screening		10(a)
2. Large Area Screening		10(a)
3. Marking/Signaling		5

Support Information on Chemical Uses and Chemicals - continued

		Types of Types
Smokes & Obscurants - cont'd.		
4.	Microwave Screening	10(a)
5.	Millimeter Wave Screening	10(a)
6.	Multispectral Screening	10(a)
7.	One Way Smoke	10(a)
8.	Standard Munitions	3
9.	Training	2
10.	Vaporization/Condensation Aerosols	2
	Total	72(a)
Synthetic Fuels		
1.	Biomass	3(a)
2.	Coal	4(a)
3.	Oil Shale	3(a)
4.	Tar Sands	3(a)
	Total	13(a)

Others - Chemicals with Undefined Types

		Estimated No. of Types	Estimated No. of Types
1.	Cosmetics	5	10
2.	Dyes	5	10
3.	Fungicides	5	10
4.	Germicides	3	6
5.	Herbicides	5	10
6.	Lubricants	5	10
7.	Pesticides	5	10
8.	Plating Material	10	10
9.	Plastic Material	5	10
10.	Rodenticides	5	10
11.	Soaps/Detergents	5	10
12.	Solvents	10	20

ENVIRONMENT CREATING WEAPONS

Aircraft	
Fixed Wing	5
Helicopter	15
Missiles	
Surface-to-Air	11
Air-to-Surface	3
Surface-to-Surface	0
Antitank/Assault	10
Weapons & Tracked Combat Vehicles	
Weapons/Other Vehicles	
Mobile Weapons	
Self-Propelled	
Antitank	1
Gun	2
Howitzer	9
Motar	7
Armored Machine Gun	6
Mines	4
Towed	
Gun	1
Howtizer	17
Other Weapons	
Flame Thrower	1
Other	4
Individual Weapons	
Personal Defense	12
Rifles	5
Individual Weapons Sights	5
Hand Grenades	5
Infantry Support	17
Other Vehicles	18
Tracked Combat Vehicles	
Main Battle Tanks	14
Air Defense Gun Carrier	1
Self-Propelled Artillery	0
Armored Command Post Vehicle	1
Armored Recovery Vehicles	5
Armored Personnel Carriers	12
Armored Reconnaissance Vehicles	3
Armored Cargo Carriers	1
Armored Combat Engineer Vehicles	1
Armored Missile Carrier	5
Infantry Fighting Vehicle	1
Cavalry Fighting Vehicle	1
	203

continued-

Environment Creating Weapons - continued

Ammunition

Plants

Active	10
Inactive	13

See also Specific Chemical Uses

Other

APPENDIX 10 CRITERIA DEVELOPMENT STEPS & COSTS

Step	Description		Price, $(000) Range	Typical
Before Testing				
1	Problem Identification Survey		10-100	25
2	Problem Definition/Literature Search		1-50	10
3	Exposure Assessment (Optional)		10-200	50
4	Environmental Fate Studies (Optional)		20-100	40
5	Analytical Methods Development (Optional)		10-500	100
6	Protocol Development (Optional)		1-40	10
7	Characterization of Chemical (Optional)		5-500	100
8	Radiolabeling and Synthesis of Test Material (Optional)		5-250	50
		Subtotal	62-1,740	385
Testing				
9	Toxicity Testing (Optional)			
	Tier 1		10-60	46
	Tier 2		250-500	350
	Tier 3		700-2,000	850
		Subtotal	960-2,560	1,246
Parallel with Testing				
10	Continuing Literature Review		10-100	50
11	Update Exposure Assessments/Fate Studies		10-100	50
12	Coordination/Liaison		50-100	75
		Subtotal	70-300	175
After Testing				
13	Criteria Document/Risk Assessment		20-100	30
14	Peer Review		1-50	10
		Subtotal	21-150	40
Operational Cost				
15	Follow-up Monitoring		1-500/yr	50/yr
16	Medical Follow-up		20-500/yr	100/yr
		Subtotal	21-1,000/yr	150/yr
Totals				
	Before Testing		62-1,740	385
	Testing		960-2,560	1,246
	Parallel with Testing		70-300	175
	After Testing		21-150	40
		Total	1,113-4,750	1,846
	Operational Cost		21-1,000/yr	150/yr

APPENDIX 11 COST BASIS FOR GENERAL TOXICOLOGY TESTS

The cost of four general toxicology tests are:

Test	Cost, ($000)	Basis
Chronic rodent inhalation	613	Table A11-1
Subchronic rodent oral	56	Table A11-2
Acute primate inhalation	39	Table A11-3
Subchronic primate inhalation	196	Table A11-4

TABLE A11-1 PROTOCOL ESTIMATE: CHRONIC RODENT TOXICOLOGY INHALATION

DIRECT LABOR PERSONNEL	Hours	Wage,$	Total $	
Study Director	240	$17.80	$ 4,272.00	
Veterinarian	60	14.00	840.00	
Compound Prep. Technician	480	6.00	2,880.00	
Senior Technician	4778	12.50	59,725.00	
Study Set Up	(93.0)			
Randomization	(46.0)			
Observations	(2000.0)			
Function Tests	(77.0)			
Record Keeping	(1360.0)			
Audit Preparation	(148.0)			
Analytical Monitoring	(1054.0)			
Animal Technician	3935	8.25	32,463.75	
Observations	(1181.0)			
Body Weights	(497.0)			
Food Consumption	(1025.0)			
Blood Collection	(61.0)			
Urine Collection	(16.0)			
Record Keeping	(867.0)			
Residue Analysis	(77.0)			
Chamber Maintenance	(211.0)			
Animal Caretaker	4325	4.00	17,300.00	
Watering	(2940.0)			
Bedding Changes	(454.0)			
Feeding	(18.0)			
Cage Cleaning	(852.0)			
Room Cleaning	(61.0)			
Clinical Lab Supervisor	52.96	10.00	529.60	
Clinical Lab Technician	158.82	6.00	952.92	
Necropsy Supervisor	116	10.00	1,160.00	
Necropsy Technician	348	5.00	1,740.00	
Histology Supervisor	252.88	10.00	2,528.80	
Histology Technician	1011.52	6.00	6,069.12	
Board Certified Pathologist	841	24.00	20,184.00	
Report Writing Supervisor	100	10.00	1,000.00	
Report Writer	1000	6.00	6,000.00	
Computer Programmer	160	8.50	1,360.00	
Computer Coder	160	5.00	800.00	
Report Typist	750	5.00	3,750.00	
General Secretary	120	6.00	720.00	
Quality Assurance Inspector	254	10.00	2,540.00	
SUBTOTAL DIRECT LABOR			$166,815.99	
Salary Adjustment (16%)			26,690.43	
TOTAL DIRECT LABOR				$193,505.62
OVERHEAD (115% of Total Direct Labor)				222,531.46

continued-

Table A11-1 - continued

OTHER DIRECT COSTS		
Overtime (683 Technician hours @$3.00)	$ 2,050.00	
(685 Caretaker hours @ $2.00)	1,370.00	
Animal Procurement (560 rats @ $3.50)	1,960.00	
Bedding (17,440 sheets @ $0.15)	2,616.00	
Animal Rations (20 g/day/rat x 10.25/50 lb)	3,202.31	
Clinical Lab Supplies (384 samples @ $9.09)	3,490.56	
Histology Supplies (23,200 samples @ $0.33)	7,656.00	
Data Processing (104 Weeks @ $50.00)	5,200.00	
Laboratory Supplies (10% of total labor)	15,172.35	
SUBTOTAL OTHER DIRECT COSTS	$ 40,467.22	
INFLATION ADJUSTMENT (20% of Other Direct Costs)	8,093.44	
TOTAL OTHER DIRECT COSTS		$ 48,560.66
TOTAL COST BEFORE G&A	$464,597.74	
G&A (10% of Total)		$ 46,459.77
TOTAL COST BEFORE FEE	$511,057.51	
FEE (20% of Total)		$102,211.50
ESTIMATED FINAL COST		$613,269.01

No actual laboratory estimates provided.

TABLE A11-2 PROTOCOL ESTIMATE: SUBCHRONIC RODENT ORAL DOSING STUDY
GENERAL TOXICOLOGY, 1 SPECIES

DIRECT LABOR PERSONNEL

	Hours	Wage,$	Total $	
Study Director	52	$17.80	$ 925.60	
Veterinarian	8	14.00	112.00	
Compound Prep. Technician	52	6.00	312.00	
Senior Technician	208.5	7.70	1,605.45	
Study Set Up	(32.0)			
Randomization	(16.0)			
Observations	(55.5)			
Blood Collection	(27.0)			
Urine Collection	(4.0)			
Record Keeping	(65.0)			
Audit Preparation	(9.0)			
Animal Technician	208.5	6.00	1,251.00	
Observations	(72.5)			
Body Weights	(35.0)			
Food Consumption	(69.0)			
Blood Collection	(27.0)			
Urine Collection	(4.0)			
Animal Caretaker	227	4.00	908.00	
Watering	(141.0)			
Bedding	(24.0)			
Feeding	(8.0)			
Cage Cleaning	(47.0)			
Room Cleaning	(7.0)			
Clinical Lab Supervisor	33.10	10.00	331.00	
Clinical Lab Technician	99.26	6.00	595.56	
Necropsy Supervisor	34	10.00	340.00	
Necropsy Technician	102	5.00	510.00	
Histology Supervisor	32.26	10.00	322.60	
Histology Technician	111.62	6.00	669.72	
Board Certified Pathologist	114	24.00	2,736.00	
Report Writing Supervisor	24	10.00	240.00	
Report Writer	320	6.00	1,920.00	
Computer Programmer	26	8.50	221.00	
Computer Coder	26	5.00	130.00	
Report Typist	300	5.00	1,500.00	
General Secretary	26	6.00	156.00	
Quality Assurance Inspector	52	10.00	520.00	
SUBTOTAL DIRECT LABOR			$ 15,305.93	
Salary Adjustment (8%)			1,224.47	
TOTAL DIRECT LABOR				$ 16,530.40
OVERHEAD (115% of Total Direct Labor)				19,009.96

Table A11-2 - continued

OTHER DIRECT COSTS		
Overtime (15 Technician hours @ $3.00)	$ 45.00	
(15 Caretaker hours @ $2.00)	30.00	
Animal Procurement (192 rats @ $3.50)	672.00	
Bedding (1600 @ $0.15)	240.00	
Animal Rations (20 g/day/rat x 10.25/50 lb)	276.75	
Clinical Lab Supplies (240 samples @ $9.09)	2,181.60	
Histology Supplies (2560 samples @ $0.33)	844.80	
Data Processing (13 weeks @ $50.00)	650.00	
Laboratory Supplies (10% of Total Labor)	1,653.04	
SUBTOTAL OTHER DIRECT COSTS	$ 6,593.19	
INFLATION ADJUSTMENT (5% of Other Direct Costs)	$ 329.66	
TOTAL OTHER DIRECT COSTS		$ 6,922.85
TOTAL COST BEFORE G&A	$ 42,463.21	
G&A (10% of Total)		$ 4,246.32
TOTAL COST BEFORE FEE	$ 46,709.53	
FEE (20% of Total)		$ 9,341.91
ESTIMATED FINAL COST		$ 56,051.44
ESTIMATED COST RANGE[a]		$28,025.72 to $84,077.16

(a) Based on laboratory survey by Enviro Control, Inc.

TABLE A11-3 PROTOCOL ESTIMATE: ACUTE PRIMATE INHALATION STUDY
GENERAL TOXICOLOGY, 1 SPECIES

Additional Assumptions

1. Using 10 Cynomalogus per dose or per control.
2. Four does levels and one control.
3. Include 20% extra animals for losses during study.

♣ Using 60 Cynomalogus

DIRECT LABOR PERSONNEL	Hours	Wage $	Total $
Study Director	2	17.80	35.60
Compound Prep. Technician	8	6.00	48.00
Senior Tech. (Inhalation)	74	12.50	925.00
Study Setup (25)			
Randomization (10)			
Observations (21)			
Body Weights (16.4)			
Record Keeping (1.75)			
Animal Tech. (Inhalation)	26.3	8.25	217.00
Body Weights (3.3)			
Dosing (16.0)			
Analytical Monitoring (7.0)			
Animal Caretaker	105.2	4.00	420.80
(60 Animals):			
Cage Cleaning (18.9)			
Room Cleaning (1.5)			
Animal Husbandry (84.8)			
Necropsy Supervisor	54	10.00	540.00
Necropsy Technician	162	5.00	810.00
Histology Supervisor	35.5	10.00	355.00
Histology Technician	148	6.00	888.00
Board-Certified Pathologist	12.2	24.00	292.80
Report Writer	32	6.00	192.00
Report Typist	20	5.00	100.00
General Secretary	1	6.00	60.00
Quality Assurance Inspector	8	10.00	80.00
TOTAL DIRECT LABOR			4892.40
OVERHEAD			5626.30

Acute Inhalation Toxicity Studies w/Primates

OTHER DIRECT COSTS	
Overtime (8 Technician hours @ $3.00)	24.00
(8 Caretaker hours @ $2.00)	16.00
Animal Procurement (60 Cynomalogus @ $300)	1800.00
Bedding (240 sheets @ 15¢)	36.00
Animal Rations (472.5g/day/Cynomalogus x 15.38/50 lbs.)	276.80

Table A11-3 - continued

OTHER DIRECT COSTS CONT'D	
Histology Supplies (150 samples @ $1.00)	$ 150.00
Laboratory Supplies (10% of Total Labor)	489.20
TOTAL OTHER DIRECT COSTS	$18,991.20
TOTAL COST BEFORE G&A	29,501.00
G&A (10% of Total)	2,950.00
TOTAL DIRECT COST BEFORE FEE	$32,451.00
FEE (20% of Total)	6,490.00
ESTIMATED FINAL COST	$38,941.00

TABLE A11-4 PROTOCOL ESTIMATE: SUBCHRONIC PRIMATE INHALATION STUDY
GENERAL TOXICOLOGY, 1 SPECIES

Assumptions

1. 90 day study
2. 20 animals per dose (10 of each sex) and 20 animals per control
3. Four dose levels (required)
4. No solvent except water - 1 control group
5. No sacrifices
6. 20% more animals for losses

Animals = 96 - same as # of rats

	Hours	Wage $	Total $
DIRECT LABOR PERSONNEL			
Study Director	96	17.80	1,708.80
Veterinarian	16	14.00	224.00
Compound Prep. Technician	96	6.00	576.00
Senior Technician (Inhalation)	929	12.50	11,613.00
Study Setup (48)			
Randomization (20)			
Observations (378)			
Dosing (233)			
Record Keeping (100)			
Audit Preparation (20)			
Analytical Monitoring (130)			
Animal Technician (Inhalation)	971	8.25	8,011.00
Body Weights (63)			
Observations (113)			
Food Consumption (240)			
Blood Collection (98)			
Urine Collection (42)			
Dosing (285)			
Analytical Monitoring (130)			
Animal Caretaker	1925	4.00	7,700.00
Cage Cleaning (397)			
Room Cleaning (32)			
Animal Husbandry (1470)			
Chamber Maintenance (26)			
Clinical Lab Supervisor	17	10.00	170.00
Clinical Lab Technician	50	6.00	300.00
Necropsy Supervisor	90	10.00	900.00
Necropsy Technician	270	5.00	1,350.00
Board-Certified Pathologist	273	24.00	6,532.00
Report Writing Supervisor	50	10.00	500.00
Report Writer	500	6.00	3,000.00
Computer Programmer	40	8.50	340.00
Computer Coder	40	5.00	200.00
Report Typist	200	5.00	1,000.00
General Secretary	40	6.00	240.00
Quality Assurance Inspector	100	10.00	1,000.00
SUBTOTAL DIRECT LABOR			44,739.00
Salary Adjustment (6%)			2,684.00

Table A11-4 - continued

TOTAL DIRECT LABOR		$ 47,423
OVERHEAD		54,537
OTHER DIRECT COSTS		
Overtime (30.2 Technician Hours @ $300)	91.00	
(227 Caretaker Hours @ $2.00)	455.00	
Animal Procurement (96 Cynomalogus @ $300)	28,800.00	
Bedding (1300 sheets @ 15¢)	195.00	
Animal Rations (472.5gm/day/Cynomalogus x 15.38/50 lbs.)	2,768.00	
Clinical Lab Supplies (560 samples @ $9.09)	5,090.00	
Histology Supplies (2960 @ $1.00)	2,960.00	
Data Processing (12 weeks @ $50.00)	600.00	
Laboratory Supplies (10% of Total Labor)	4,474.00	
SUBTOTAL OTHER DIRECT COSTS	45,433.00	
INFLATION ADJUSTED OTHER DIRECT COSTS (2.5%)		$ 46,596
TOTAL COST BEFORE G&A		148,529
G&A (10% of Total)		14,853
TOTAL COST BEFORE FEE		$163,382
FEE (20% of Total)		32,676
ESTIMATED FINAL COST		$195,058

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